- STN SEARCH TRANSCRIPT - 10/800,328

MEDLINE ENABLEMENT

SEARCH FOR CLAIMED METHODS-OF-TREATMENT

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1623zct

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

```
NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
NEWS  2          "Ask CAS" for self-help around the clock
NEWS  3  DEC 18  CA/CAplus pre-1967 chemical substance index entries enhanced
                 with preparation role
NEWS  4  DEC 18  CA/CAplus patent kind codes updated
NEWS  5  DEC 18  MARPAT to CA/CAplus accession number crossover limit increased
                 to 50,000
NEWS  6  DEC 18  MEDLINE updated in preparation for 2007 reload
NEWS  7  DEC 27  CA/CAplus enhanced with more pre-1907 records
NEWS  8  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS  9  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 10  JAN 16  IPC version 2007.01 thesaurus available on STN
NEWS 11  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 12  JAN 22  CA/CAplus updated with revised CAS roles
NEWS 13  JAN 22  CA/CAplus enhanced with patent applications from India
NEWS 14  JAN 29  PHAR reloaded with new search and display fields
NEWS 15  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                 multiple databases
NEWS 16  FEB 15  PATDPASPC enhanced with Drug Approval numbers
NEWS 17  FEB 15  RUSSIAPAT enhanced with pre-1994 records
NEWS 18  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
NEWS 19  FEB 26  MEDLINE reloaded with enhancements
NEWS 20  FEB 26  EMBASE enhanced with Clinical Trial Number field
NEWS 21  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
NEWS 22  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 23  FEB 26  CAS Registry Number crossover limit increased from 10,000
                 to 300,000 in multiple databases
NEWS 24  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 25  MAR 16  CASREACT coverage extended
NEWS 26  MAR 20  MARPAT now updated daily
NEWS 27  MAR 22  LWPI reloaded
NEWS 28  MAR 30  RDISCLOSURE reloaded with enhancements
NEWS 29  MAR 30  INPADOCDB will replace INPADOC on STN
NEWS 30  APR 02  JICST-EPLUS removed from database clusters and STN

NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS LOGIN    Welcome Banner and News Items
NEWS IPC8     For general information regarding STN implementation of IPC 8
NEWS X25      X.25 communication option no longer available
```

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:29:16 ON 09 APR 2007

=> FILE MEDLINE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 12:29:27 ON 09 APR 2007

FILE LAST UPDATED: 7 Apr 2007 (20070407/UP). FILE COVERS 1950 TO DATE.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> S BRIGHT
          9184 BRIGHT
             2 BRIGHTS
L1        9185 BRIGHT
               (BRIGHT OR BRIGHTS)

=> S L1 AND ANTIPSYCHOTICS
          5343 ANTIPSYCHOTICS
L2           1 L1 AND ANTIPSYCHOTICS

=> D

L2   ANSWER 1 OF 1     MEDLINE on STN
AN   2005667736     MEDLINE
DN   PubMed ID: 16354123
TI   Pharmacogenomics: a path to predictive medicine for schizophrenia.
AU   Gupta Simone; Jain Sanjeev; Brahmachari Samir K; Kukreti Ritushree
CS   Institute of Genomics and Integrative Biology (CSIR), Delhi University
     Campus, Delhi 110007, India.
SO   Pharmacogenomics, (2006 Jan) Vol. 7, No. 1, pp. 31-47.  Ref: 159
     Journal code: 100897350. ISSN: 1462-2416.
CY   England: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
     (RESEARCH SUPPORT, NON-U.S. GOV'T)
     General Review; (REVIEW)
LA   English
FS   Priority Journals
EM   200602
ED   Entered STN: 20 Dec 2005
     Last Updated on STN: 28 Feb 2006
     Entered Medline: 27 Feb 2006


=> D ABS

L2   ANSWER 1 OF 1     MEDLINE on STN
AB   A significant variability is observed among patients in response to
     antipsychotics, and is caused by a variety of factors.  This
     review summarizes the available knowledge of associations between
     pharmacogenetics and drug response in schizophrenia.  The multifactorial
     etiology of schizophrenia makes it a complex interaction of symptoms.
     Adopting a pharmacogenomics approach represents a unique opportunity for
     the prediction of response to antipsychotic drugs by investigating genes
     implicated with specific symptoms and side effects.  A network model of
     the interaction/crosstalk between the neurotransmitter signaling systems
```

is presented to emphasize the importance of the genes associated with the molecular mechanisms of the disease and drug response. These genes may serve as potential susceptibility genes and drug targets for schizophrenia. The crucial point for the identification of a significant biologic marker(s) will include not only the experimental validation of the genes involved in the neurotransmitter signaling systems, but also the availability of large exactly comparable phenotyped patients samples. Coupling our knowledge of genetic polymorphisms with clinical response data promises a bright future for rapid advances in personalized medicine.

```
=> E BRIGHT GENE MICHAEL/AU 25
E1          17     BRIGHT G R/AU
E2           1     BRIGHT GAERTNER E/AU
E3           0 --> BRIGHT GENE MICHAEL/AU
E4           1     BRIGHT GEORGE M/AU
E5           7     BRIGHT H/AU
E6          57     BRIGHT H J/AU
E7           3     BRIGHT H L/AU
E8           2     BRIGHT HELEN/AU
E9           1     BRIGHT HOWARD/AU
E10          1     BRIGHT I/AU
E11          4     BRIGHT I B/AU
E12          1     BRIGHT ISAAC J/AU
E13         36     BRIGHT J/AU
E14         30     BRIGHT J E/AU
E15          1     BRIGHT J F/AU
E16          1     BRIGHT J I/AU
E17         20     BRIGHT J J/AU
E18          5     BRIGHT J L/AU
E19         33     BRIGHT J M/AU
E20          2     BRIGHT J N/AU
E21          7     BRIGHT J R/AU
E22          5     BRIGHT J S/AU
E23          2     BRIGHT JAMES E H/AU
E24          1     BRIGHT JANE H/AU
E25          8     BRIGHT JANICE M/AU

=> E WLODECKI BISHOP/AU 25
E1           1     WLODAWETZ V W/AU
E2           1     WLODECKA I/AU
E3           0 --> WLODECKI BISHOP/AU
E4           2     WLODEK A/AU
E5           1     WLODEK AGATA/AU
E6           3     WLODEK B/AU
E7          23     WLODEK D/AU
E8           1     WLODEK DANUTA/AU
E9           1     WLODEK G/AU
E10          1     WLODEK G D/AU
E11         13     WLODEK G K/AU
E12          1     WLODEK J/AU
E13         23     WLODEK L/AU
E14          2     WLODEK L B/AU
E15         17     WLODEK LIDIA/AU
E16          1     WLODEK LIDIA B/AU
E17          2     WLODEK M/AU
E18         38     WLODEK M E/AU
E19          1     WLODEK MARY/AU
E20          6     WLODEK MARY E/AU
E21          1     WLODEK P J/AU
E22          1     WLODEK PRZEMYSLAW/AU
E23          2     WLODEK PRZEMYSLAW J/AU
E24          3     WLODEK S/AU
E25          6     WLODEK S T/AU
```

```
=> E BRODNEY MICHAEL A/AU 25
E1           1     BRODNEY K/AU
E2           3     BRODNEY M A/AU
E3           1 --> BRODNEY MICHAEL A/AU
E4           3     BRODNEY S/AU
E5           4     BRODNIAK W/AU
E6           2     BRODNIAK WLODZIMIERZ A/AU
E7           3     BRODNICK D/AU
E8           1     BRODNICK D E/AU
E9           1     BRODNICK DONALD E/AU
E10          1     BRODNICK M S/AU
E11          2     BRODNICK S/AU
E12          1     BRODNICKA A/AU
E13          2     BRODNICKA L/AU
E14          3     BRODNICKI T/AU
E15          7     BRODNICKI T C/AU
E16          2     BRODNICKI THOMAS/AU
E17          8     BRODNICKI THOMAS C/AU
E18          9     BRODNIEWICZ A/AU
E19         10     BRODNIEWICZ PROBA T/AU
E20          3     BRODNIEWICZ T/AU
E21         14     BRODNIEWICZ Z/AU
E22          2     BRODNIG V/AU
E23          1     BRODNIK ISABELLA/AU
E24          8     BRODNIK M/AU
E25          1     BRODNIK M M/AU

=> S E3
L3           1 "BRODNEY MICHAEL A"/AU

=> D IBIB ABS

L3   ANSWER 1 OF 1      MEDLINE on STN
ACCESSION NUMBER:    2004255135      MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15153003
TITLE:               A new strategy toward indole alkaloids involving an
                     intramolecular cycloaddition/rearrangement cascade.
AUTHOR:              Padwa Albert; Brodney Michael A; Lynch Stephen M;
                     Rashatasakhon Paitoon; Wang Qiu; Zhang Hongjun
CORPORATE SOURCE:    Department of Chemistry, Emory University, Atlanta, Georgia
                     30322, USA.. chemap@emory.edu
SOURCE:              The Journal of organic chemistry, (2004 May 28) Vol. 69,
                     No. 11, pp. 3735-45.
                     Journal code: 2985193R. ISSN: 0022-3263.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200409
ENTRY DATE:          Entered STN: 22 May 2004
                     Last Updated on STN: 21 Sep 2004
                     Entered Medline: 17 Sep 2004
AB   The intramolecular Diels-Alder reaction between an amidofuran moiety
     tethered onto an indole component was examined as a strategy for the
     synthesis of Aspidosperma alkaloids. Furanyl carbamate 23 was acylated
     using the mixed anhydride 26 to provide amidofuran 22 in 68% yield.
     Further N-acylation of this indole furnished 27 in 88% yield. Cyclization
     precursors were prepared by removing the carbamate moiety followed by
     N-alkylation with the appropriate alkyl halides. Large substituent groups
     on the amido nitrogen atom causes the reactive s-trans conformation of the
     amidofuran to be more highly populated, thereby facilitating the
     Diels-Alder cycloaddition. The reaction requires the presence of an
     electron-withdrawing substituent on the indole nitrogen in order for the
```

cycloaddition to proceed. Treatment of N-allyl-bromoenamide 48 with n-Bu(3)SnH/AIBN preferentially led to the 6-endo trig cyclization product 50, with the best yield (91%) being obtained under high dilution conditions. The initially generated cyclohexenyl radical derived from 48 produces the pentacyclic heterocycle 50 by either a direct 6-endo trig cyclization or, alternatively, by a vinyl radical rearrangement pathway.

```
=> S ANTAGONISTS AND (5HT1B OR 5HT2A OR D2)
        487496 ANTAGONISTS
           137 5HT1B
           179 5HT2A
         26201 D2
L4         6832 ANTAGONISTS AND (5HT1B OR 5HT2A OR D2)

=> S L4 AND 2003/PY
        569314 2003/PY
                (20030000-20039999/PY)
L5          349 L4 AND 2003/PY

=> S L5 AND REVIEW
        475081 REVIEW
         59625 REVIEWS
        520853 REVIEW
                (REVIEW OR REVIEWS)
L6            7 L5 AND REVIEW

=> D 1-7 IBIB ABS

L6   ANSWER 1 OF 7     MEDLINE on STN
ACCESSION NUMBER:   2004019152     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 14715440
TITLE:              Novel mechanisms and approaches in the study of
                    neurodegeneration and neuroprotection. a review.
AUTHOR:             Kostrzewa Richard M; Segura-Aguilar Juan
CORPORATE SOURCE:   Department of Pharmacology, Quillen College of Medicine,
                    East Tennessee State University, Johnson City, TN 37614,
                    USA.. kostrzew@etsu.edu
CONTRACT NUMBER:    NS 39272 (NINDS)
SOURCE:             Neurotoxicity research, (2003) Vol. 5, No. 6, pp.
                    375-83.  Ref: 93
                    Journal code: 100929017. ISSN: 1029-8428.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200402
ENTRY DATE:         Entered STN: 13 Jan 2004
                    Last Updated on STN: 3 Feb 2004
                    Entered Medline: 2 Feb 2004
```

AB Cellular mechanisms involved in neurodegeneration and neuroprotection are continuing to be explored, and this paper focuses on some novel discoveries that give further insight into these processes. Oligodendrocytes and activated astroglia are likely generators of the pro-inflammatory cytokines, such as the tumor necrosis factor family and interleukin family, and these glial support cells express adhesion receptors (e.g., VCAM) and release intercellular adhesion molecules (ICAM) that have a major role in neuronal apoptosis. Even brief exposure to some substances, in ontogeny and sometimes in adulthood, can have lasting effects on behaviors because of their prominent toxicity (e.g., NMDA receptor antagonists) or because they sensitize receptors (e.g., dopamine D2 agonists), possibly permanently, and thereby alter behavior for the lifespan. Cell cycle genes which may be derived from microglia, are the most-recent entry into the neuroprotection schema. Neuroprotection afforded by some common substances (e.g., melatonin) and uncommon substances [e.g., nicotine, green tea polyphenol (-)-epigallocatechin-3-gallate (EGCG), trolox], ordinarily thought to be simple radical scavengers, now are thought to invoke previously unsuspected cellular mechanisms in the process of neuroprotection. Although Alzheimer's disease (AD) has features of a continuous spectrum of neural and functional decline, in vivo PET imaging and and functional magnetic resonance imaging, indicate that AD can be staged into an early phase treatable by inhibitors of beta and gamma secretase; and a late phase which may be more amenable to treatment by drugs that prevent or reverse tau phosphorylation. Neural transplantation, thought to be the last hope for neurally injured patients (e.g., Parkinsonians), may be displaced by non-neural tissue transplants (e.g., human umbilical cord blood; Sertoli cells) which seem to provide similar neurotrophic support and improved behavior - without posing the major ethical dilemma of removing tissue from aborted fetuses. The objective of this paper is to invite added research into the newly discovered (or postulated) novel mechanisms; and to stimulate discovery of additional mechanisms attending neurodegeneration and neuroprotection.

```
L6   ANSWER 2 OF 7     MEDLINE on STN
ACCESSION NUMBER:   2003582573     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 14663001
TITLE:              Adenosine-dopamine interactions: development of a concept
                    and some comments on therapeutic possibilities.
AUTHOR:             Fredholm Bertil B; Svenningsson Per
CORPORATE SOURCE:   Department of Physiology and Pharmacology, Karolinska
                    Institutet, Stockholm, Sweden.. Bertil.Fredholm@fyfa.ki.se
SOURCE:             Neurology, (2003 Dec 9) Vol. 61, No. 11 Suppl 6,
                    pp. S5-9.  Ref: 63
                    Journal code: 0401060. E-ISSN: 1526-632X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        200402
ENTRY DATE:         Entered STN: 16 Dec 2003
                    Last Updated on STN: 12 Feb 2004
                    Entered Medline: 11 Feb 2004
```

AB This brief review presents a personal perspective on the historical development of the current knowledge about the biologically important concept of functional antagonism between adenosine A2A and dopamine D2 receptors in caudate-putamen, accumbens, and tuberculum olfactorium. In the 1970s, studies of dopamine actions suggested an unexpected role of adenosine. Developments during the next decade substantiated this finding and demonstrated that a subform of adenosine A2 receptors was enriched in the basal ganglia. Cloning of adenosine receptors provided better tools for cellular localization and showed that A2A receptors are closely associated with D2 receptors. Distinct functional interactions at several levels were discovered, and there is now strong evidence that A2A receptors are tonically active and modified by dopamine acting at D2 receptors. Development of selective antagonists and knockout mice have highlighted the potential usefulness of A2A antagonists in decreasing symptoms and progression of Parkinson's disease-something that has also been vindicated by careful epidemiologic studies. There are issues of efficacy and potential side effects that need to be resolved, but the future looks bright.

```
L6   ANSWER 3 OF 7     MEDLINE on STN
ACCESSION NUMBER:   2003565927     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 14647530
```

TITLE: Neuropharmacological profile of an atypical antipsychotic, NRA0562.
AUTHOR: Hirota Shiho; Kawashima Naoya; Chaki Shigeyuki; Okuyama Shigeru
CORPORATE SOURCE: Psychiatric Diseases and Pain Research, Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., 1-403 Yoshino-cho, Kita-ku, Saitama, Saitama 331-9530, Japan.. shiho.hirota@po.rd.taisho.co.jp
SOURCE: CNS drug reviews, (2003 Winter) Vol. 9, No. 4, pp. 375-88. Ref: 70
Journal code: 9514898. ISSN: 1080-563X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 21 Jan 2004
Entered Medline: 20 Jan 2004

AB Schizophrenia is a serious and disabling psychiatric disorder affecting approximately 1% of the world's population. A new generation of atypical antipsychotics has been introduced over the past decade. These atypical antipsychotics have comparable or greater efficacy than traditional antipsychotics in the treatment of the psychotic symptoms of schizophrenia and a much improved neurologic side effect profile. This paper reviews the pharmacological efficacy and safety of a potential atypical antipsychotic, NRA0562. NRA0562 has a high affinity for dopamine D1, D2L, D4.2, 5-HT2A receptors as well as alpha1-adrenoceptors, and has a moderate affinity for H1 receptors. NRA0562 strongly binds to 5-HT2A receptors and alpha1-adrenoceptors in the frontal cortex, its binding to striatal D2 receptors is weaker, similar to that of clozapine. NRA562 displayed potent antipsychotic activities in animal models of schizophrenia, such as methamphetamine (MAP)-induced hyperactivity, apomorphine-induced disruption of pre-pulse inhibition and conditioned avoidance test. NRA0562 is more potent in reversing the inhibitory effects of MAP at A10 than at A9 dopamine neurons. It increased Fos-like immunoreactivity in the nucleus accumbens more effectively than in the dorsolateral striatum, indicating that NRA0562 has the profile of an atypical antipsychotic. In vivo assays for extrapyramidal side effect liability showed that NRA0562 has a low rate of neurological side effects. Thus, NRA0562 may have unique antipsychotic activity with a lower propensity for extrapyramidal side effects.

L6 ANSWER 4 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2003533618 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14612145
TITLE: Rapid regulation of dopamine transporter function by substrates, blockers and presynaptic receptor ligands.
AUTHOR: Gulley Joshua M; Zahniser Nancy R
CORPORATE SOURCE: Department of Pharmacology and Neuroscience Program, University of Colorado Health Sciences Center, Campus Box C-236, 4200 E Ninth Avenue, Denver, CO 80262, USA.. joshua.gulley@uchsc.edu
CONTRACT NUMBER: DA 04216 (NIDA)
DA 15050 (NIDA)
SOURCE: European journal of pharmacology, (2003 Oct 31) Vol. 479, No. 1-3, pp. 139-52. Ref: 140
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 13 Nov 2003
Last Updated on STN: 21 Jul 2004
Entered Medline: 20 Jul 2004

AB The extracellular actions of dopamine are terminated primarily through its binding to dopamine transporters and translocation back into dopamine neurons. The transporter thereby serves as an optimal target to regulate dopamine neurotransmission. Although acute pharmacological blockade of dopamine transporters is known to reversibly inhibit transporter function by preventing the binding of its endogenous substrate dopamine, it recently has become clear that dopamine transporter substrates, such as amphetamines, and blockers, such as cocaine, also have the ability to rapidly and persistently regulate transporter function after their direct pharmacological effect has subsided. Presynaptic receptor ligands can also regulate dopamine transporter function. This has been investigated most extensively for dopamine D2 receptors, but there is also evidence for regulation by gamma-aminobutyric acid (GABA) GABAB receptors, metabotropic glutamate, nicotinic acetylcholine, serotonin, sigma2- and kappa-opioid receptors. The focus of this review is the rapid, typically reversible, regulation of dopamine transporter velocity by substrates, blockers and presynaptic receptor ligands. The research discussed here suggests that a common mechanism through which these different classes of compounds regulate transporter activity is by altering the cell surface expression of dopamine transporters.

L6 ANSWER 5 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2003364198 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12895600
TITLE: The second PGD(2) receptor CRTH2: structure, properties, and functions in leukocytes.
AUTHOR: Nagata Kinya; Hirai Hiroyuki
CORPORATE SOURCE: R&D Centre, Bio Medical Laboratories, Inc, 1361-1 Matoba, Kawagoe, Saitama 350-1101, Japan.. nagata@alk.co.jp
SOURCE: Prostaglandins, leukotrienes, and essential fatty acids, (2003 Aug-Sep) Vol. 69, No. 2-3, pp. 169-77. Ref: 76
Journal code: 8802730. ISSN: 0952-3278.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 5 Aug 2003
Last Updated on STN: 17 Apr 2004
Entered Medline: 16 Apr 2004

AB Prostaglandin (PG) D(2) plays a broad range of physiological and pathophysiological functions. Until just a few years ago, it was thought that most of the biological actions of PGD(2) are mediated via the classical PGD(2) receptor DP. Recently, we identified a second PGD(2) receptor, chemoattractant receptor-homologous molecule expressed on T helper (Th)2 cells (CRTH2), with different functions relative to DP. Here, we review the recent findings on the structure, tissue distribution, ligand selectivity, signalling pathways, and functions in leukocytes of this receptor. The data suggest that the PGD(2)/CRTH2 system play important roles in allergic inflammation through its stimulatory effects on Th2 cells, eosinophils, and basophils.

L6 ANSWER 6 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2003288164 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12814658
TITLE: Targeting striatal cholinergic interneurons in Parkinson's disease: focus on metabotropic glutamate receptors.

AUTHOR: Pisani A; Bonsi P; Centonze D; Gubellini P; Bernardi G; Calabresi P
CORPORATE SOURCE: Clinica Neurologica, Dipartimento di Neuroscienze, Universita di Roma Tor Vergata, Rome, Italy.. pisani@uniroma2.it
SOURCE: Neuropharmacology, (2003 Jul) Vol. 45, No. 1, pp. 45-56. Ref: 95
Journal code: 0236217. ISSN: 0028-3908.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20 Jun 2003
Last Updated on STN: 12 Aug 2003
Entered Medline: 11 Aug 2003

AB In the early sixties, anticholinergic drugs were introduced in the pharmacological treatment of Parkinson's disease (PD). The rationale behind their utilisation in the treatment of the disease was based on the evidence of an imbalance between the dopaminergic inputs and the intrinsic cholinergic innervation within the striatum. Metabotropic glutamate (mGlu) receptors have been shown to play a key role in striatal function both in physiological conditions and in experimental models of diseases affecting this brain area. Indeed, compelling electrophysiological and morphological evidence shows that mGlu receptors are highly expressed at cellular level and exert a profound modulatory role on cholinergic interneurons excitability. This review will provide a brief survey of studies on the localization and function of mGlu receptors in cholinergic interneurons. The potential relevance of these findings in the control of motor function and in the treatment of PD will be discussed.

L6 ANSWER 7 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2003275541 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12801600
TITLE: Neurotensin: dual roles in psychostimulant and antipsychotic drug responses.
AUTHOR: Dobner Paul R; Deutch Ariel Y; Fadel Jim
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Program in Neuroscience, University of Massachusetts Medical School, 55 Lake Ave. North, Worcester 01655, USA.. paul.dobner@umassmed.edu
CONTRACT NUMBER: HL-33307 (NHLBI)
MH-45124 (NIMH)
MH-57795 (NIMH)
NS-44282 (NINDS)
SOURCE: Life sciences, (2003 Jun 27) Vol. 73, No. 6, pp. 801-11. Ref: 82
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 13 Jun 2003
Last Updated on STN: 18 Jul 2003
Entered Medline: 17 Jul 2003

AB Central administration of neurotensin (NT) results in a variety of neurobehavioral effects which, depending upon the administration site, resemble the effects of antipsychotic drugs (APDs) and psychostimulants. All clinically effective APDs exhibit significant affinities for dopamine D(2) receptors, supporting the hypothesis that an increase in dopaminergic tone contributes to schizophrenic symptoms. Psychostimulants increase extracellular dopamine (DA) levels and chronics administration can produce psychotic symptoms over time. APDs and psychostimulants induce Fos and NT expression in distinct striatal subregions, suggesting that changes in gene expression underlie some of their effects. To gain insight into the functions of NT, we analyzed APD and psychostimulant induction of Fos in NT knockout mice and rats pretreated with the NT antagonist SR 48692. In both NT knockout mice and rats pretreated with SR 48692, haloperidol-induced Fos expression was markedly attenuated in the dorsolateral striatum; amphetamine-induced Fos expression was reduced in the medial striatum. These results indicate that NT is required for the activation of specific subpopulations of striatal neurons in distinct striatal subregions in response to both APDs and psychostimulants. This review integrates these new findings with previous evidence implicating NT in both APD and psychostimulant responses.

=>
=> FILE REG
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 15.24 15.45

FILE 'REGISTRY' ENTERED AT 12:49:42 ON 09 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 APR 2007 HIGHEST RN 929518-97-8
DICTIONARY FILE UPDATES: 8 APR 2007 HIGHEST RN 929518-97-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> S NRA0562/CN
L7 0 NRA0562/CN

=> S NRA0562
L8 0 NRA0562

=> SEL 3
L8 HAS NO ANSWERS
An L-number has no answers for one of five reasons:
1. It is a query that has not been searched, or
2. It is the result of a search with zero answers, or
3. It is an intermediate result of the ACTIVATE command, or
4. It is an intermediate result in SEARCH STEPS, or
5. It is an L-number created by the RUN command

```
=> SEL L6 3
NO ANSWERS SELECTED.  THE ANSWER SET WAS CREATED IN FILE 'MEDLINE'.
USE THE FILE COMMAND TO CHANGE TO THE CORRECT FILE.
An answer set can be processed to create terms only
in the same file in which it was created.

=> FILE MEDLINE
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                10.80      26.25

FILE 'MEDLINE' ENTERED AT 12:50:36 ON 09 APR 2007

 FILE LAST UPDATED: 7 Apr 2007 (20070407/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> SEL L6 3
E1 THROUGH E7 ASSIGNED

=> FIL STNGUIDE
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.39      26.64

FILE 'STNGUIDE' ENTERED AT 12:51:24 ON 09 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr  6, 2007 (20070406/UP).

=> FILE MEDLINE
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.06      26.70

FILE 'MEDLINE' ENTERED AT 12:52:14 ON 09 APR 2007

 FILE LAST UPDATED: 7 Apr 2007 (20070407/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> D E1-E7
'E1-E7' IS NOT A VALID ACCESSION NUMBER

The number entered is not a valid accession number in this file.
Enter "HELP ACCESSION" at an arrow prompt (=>) for a list of valid
accession number formats in the current file.

=> S 2003565927/AN
L9             1 2003565927/AN

=> D

L9   ANSWER 1 OF 1     MEDLINE on STN
AN   2003565927     MEDLINE
DN   PubMed ID: 14647530
TI   Neuropharmacological profile of an atypical antipsychotic, NRA0562.
AU   Hirota Shiho; Kawashima Naoya; Chaki Shigeyuki; Okuyama Shigeru
CS   Psychiatric Diseases and Pain Research, Medicinal Pharmacology Laboratory,
     Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., 1-403
     Yoshino-cho, Kita-ku, Saitama, Saitama 331-9530, Japan..
     shiho.hirota@po.rd.taisho.co.jp
SO   CNS drug reviews, (2003 Winter) Vol. 9, No. 4, pp. 375-88.  Ref: 70
     Journal code: 9514898. ISSN: 1080-563X.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
     General Review; (REVIEW)
LA   English
FS   Priority Journals
EM   200401
ED   Entered STN: 16 Dec 2003
     Last Updated on STN: 21 Jan 2004
     Entered Medline: 20 Jan 2004


=> SEL RN
E8 THROUGH E8 ASSIGNED

=> D E8
'E8' IS NOT A VALID FORMAT FOR FILE 'MEDLINE'

The following are valid formats:

The default display format is BIB.

ABS ---- AB
ALL ---- AN, DN, TI, AU, CS, NC, SO, CM, CY, DT, LA, FS, NCT, OS,
         EM, ED, AB, ST, CT, NA, RN, CN, GEN
BIB ---- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
CBIB --- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
DALL --- ALL, delimited for post processing
IABS --- ABS, with a text label
IALL --- ALL, indented with text labels
IBIB --- BIB, indented with text labels
IND ---- ST, CT, NA, RN, CN, GEN
TRIAL -- TI, ST, CT, NA, RN, CN, GEN
  (SAM, TRI, FREE)
HIT ---- All fields containing hit terms
HITIND - IND
KWIC --- All hit terms plus 20 words on either side
OCC ---- List of display fields containing hit terms

Hit terms will be highlighted in all available fields except CM and
PY.

To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'BIB';
'AB'; 'SO,ST'.  You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.
ENTER DISPLAY FORMAT (BIB):END

=> FILE REG
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.56      27.26

FILE 'REGISTRY' ENTERED AT 12:53:04 ON 09 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
```

COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 APR 2007 HIGHEST RN 929518-97-8
DICTIONARY FILE UPDATES: 8 APR 2007 HIGHEST RN 929518-97-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

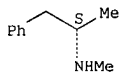
http://www.cas.org/ONLINE/UG/regprops.html

=> S E8
L10 1 537-46-2/BI
(537-46-2/RN)

=> D

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 537-46-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzeneethanamine, N,α-dimethyl-, (αS)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneethanamine, N,α-dimethyl-, (S)-
CN Phenethylamine, N,α-dimethyl-, (S)-(+)- (8CI)
OTHER NAMES:
CN (+)-(S)-Deoxyephedrine
CN (+)-2-(N-Methylamino)-1-phenylpropane
CN (+)-Methamphetamine
CN (+)-Methylamphetamine
CN (+)-N,α-Dimethyl-β-phenylethylamine
CN (+)-N-Methylamphetamine
CN (S)-(+)-Deoxyephedrine
CN (S)-(+)-Methamphetamine
CN (S)-Methamphetamine
CN (S)-Methylamphetamine
CN 2S-(+)-Methamphetamine
CN Corvitin
CN d-(S)-Methamphetamine
CN d-Deoxyephedrine
CN d-Desoxyephedrine
CN d-Methamphetamine
CN d-Methylamphetamine
CN d-N,α-Dimethylphenethylamine
CN d-N-Methylamphetamine
CN d-Phenylisopropylmethylamine
CN L-Methamphetamine
CN Metamfetamine
CN Metamphetamine
CN Methamphetamine
CN Methyl-β-phenylisopropylamine
CN Methylamphetamine
CN N-Methyl-1-phenyl-2-propanamine
CN N-Methylamphetamine
CN Norodin
CN NSC 25115
FS STEREOSEARCH
DR 139-47-9, 1690-86-4, 14611-50-8, 45952-89-4
MF C10 H15 N
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PIRA, PROMT, PS, RTECS*, SCISEARCH, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4580 REFERENCES IN FILE CA (1907 TO DATE)
100 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4597 REFERENCES IN FILE CAPLUS (1907 TO DATE)
19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> LOG HOLD

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	3.75	31.01

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 12:55:36 ON 09 APR 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1623zct

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'REGISTRY' AT 13:04:58 ON 09 APR 2007
FILE 'REGISTRY' ENTERED AT 13:04:58 ON 09 APR 2007
COPYRIGHT (C) 2007 American Chemical Society (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	3.75	31.01

=> FILE 2002/PY
'2002/PY' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'REGISTRY'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

```
=> FILE MEDLINE
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         4.20      31.46

FILE 'MEDLINE' ENTERED AT 13:05:22 ON 09 APR 2007

 FILE LAST UPDATED: 7 Apr 2007 (20070407/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> S 2002/PY
L11      542785 2002/PY
                (20020000-20029999/PY)

=> S L11 AND REVIEW
         475081 REVIEW
          59625 REVIEWS
         520853 REVIEW
                (REVIEW OR REVIEWS)
L12       30323 L11 AND REVIEW

=> S L12 AND BENZISOXAZOLE
            116 BENZISOXAZOLE
             20 BENZISOXAZOLES
            130 BENZISOXAZOLE
                (BENZISOXAZOLE OR BENZISOXAZOLES)
L13           0 L12 AND BENZISOXAZOLE

=> S BENZISOXAZOLE AND 2003/PY
            116 BENZISOXAZOLE
             20 BENZISOXAZOLES
            130 BENZISOXAZOLE
                (BENZISOXAZOLE OR BENZISOXAZOLES)
         569314 2003/PY
                (20030000-20039999/PY)
L14           5 BENZISOXAZOLE AND 2003/PY

=> D 1-5

L14  ANSWER 1 OF 5     MEDLINE on STN
AN   2003569076     MEDLINE
DN   PubMed ID: 14640551
TI   1,2-benzisoxazole phosphorodiamidates as novel anticancer
     prodrugs requiring bioreductive activation.
AU   Jain Monish; Kwon Chul-Hoon
CS   Department of Pharmaceutical Sciences, College of Pharmacy and Allied
     Health Professions, St John's University, Jamaica, New York 11439, USA.
SO   Journal of medicinal chemistry, (2003 Dec 4) Vol. 46, No. 25,
     pp. 5428-36.
     Journal code: 9716531. ISSN: 0022-2623.
CY   United States
DT   (IN VITRO)
     Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200401
ED   Entered STN: 16 Dec 2003
     Last Updated on STN: 17 Jan 2004
     Entered Medline: 16 Jan 2004

L14  ANSWER 2 OF 5     MEDLINE on STN
AN   2003405077     MEDLINE
DN   PubMed ID: 12944663
TI   2-(2,1-benzoxazol-3-yl)-3,5-dimethoxyphenol and 3-phenyl-2,1-benzoxazole.
AU   Howie R Alan; Jabbar Abdul; Lewis John R; Nizami Shaikh S; Ritchie Craig F
CS   Department of Chemistry, University of Aberdeen, Meston Walk, Aberdeen
     AB24 3UE, Scotland.. r.a.howie@abdn.ac.uk
SO   Acta crystallographica. Section C, Crystal structure communications,
     (2003 Sep) Vol. 59, No. Pt 9, pp. o516-9.  Electronic Publication:
     2003-08-09.
     Journal code: 8305826. ISSN: 0108-2701.
CY   Denmark
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   NONMEDLINE; PUBMED-NOT-MEDLINE
EM   200402
ED   Entered STN: 29 Aug 2003
     Last Updated on STN: 2 Mar 2004
     Entered Medline: 26 Feb 2004

L14  ANSWER 3 OF 5     MEDLINE on STN
AN   2003335232     MEDLINE
DN   PubMed ID: 12867488
TI   Substituent effect on the reductive N-dearylation of 3-(indol-1-yl)-1,2-
     benzisoxazoles by rat liver microsomes.
AU   Tschirret-Guth Richard A; Wood Harold B
CS   Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ
     07065, USA.. richard_tschirretguth@merck.com
SO   Drug metabolism and disposition: the biological fate of chemicals,
     (2003 Aug) Vol. 31, No. 8, pp. 999-1004.
     Journal code: 9421550. ISSN: 0090-9556.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200406
ED   Entered STN: 18 Jul 2003
     Last Updated on STN: 18 Jun 2004
     Entered Medline: 17 Jun 2004

L14  ANSWER 4 OF 5     MEDLINE on STN
AN   2003141915     MEDLINE
DN   PubMed ID: 12657263
TI   Phenylacetic acid derivatives as hPPAR agonists.
AU   Santini Conrad; Berger Gregory D; Han Wei; Mosley Ralph; MacNaul Karen;
     Berger Joel; Doebber Thomas; Wu Margaret; Moller David E; Tolman Richard
     L; Sahoo Soumya P
CS   Department of Basic Chemistry, Merck Research Laboratories, Rahway, NJ
     07065, USA.. conrad_santini@merck.com
SO   Bioorganic & medicinal chemistry letters, (2003 Apr 7) Vol. 13,
     No. 7, pp. 1277-80.
     Journal code: 9107377. ISSN: 0960-894X.
CY   England: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200311
ED   Entered STN: 27 Mar 2003
     Last Updated on STN: 4 Nov 2003
     Entered Medline: 3 Nov 2003

L14  ANSWER 5 OF 5     MEDLINE on STN
AN   2003073789     MEDLINE
DN   PubMed ID: 12583727
TI   Isoxazole --> benzisoxazole rearrangement promoted cascade
     reactions affording stereodefined polycycles.
AU   Bode Jeffrey W; Uesuka Hidehiro; Suzuki Keisuke
```

CS Department of Chemistry, Tokyo Institute of Technology, and CREST, Japan Science and Technology (JST) Corporation, O-okayama, Meguro-ku, Tokyo 152-8551, Japan.
SO Organic letters, (2003 Feb 20) Vol. 5, No. 4, pp. 395-8.
Journal code: 100890393. ISSN: 1523-7060.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; PUBMED-NOT-MEDLINE
EM 200307
ED Entered STN: 14 Feb 2003
Last Updated on STN: 17 Jul 2003
Entered Medline: 16 Jul 2003

=> S BENZISOXAZOLE AND (D2 OR 5HT1B OR 5HT2B OR 5HT-1A OR 5HT-2B)
116 BENZISOXAZOLE
20 BENZISOXAZOLES
130 BENZISOXAZOLE
(BENZISOXAZOLE OR BENZISOXAZOLES)
26201 D2
137 5HT1B
11 5HT2B
2604 5HT
19985 1A
104 5HT-1A
(5HT(W)1A)
2604 5HT
17924 2B
3 5HT-2B
(5HT(W)2B)
L15 14 BENZISOXAZOLE AND (D2 OR 5HT1B OR 5HT2B OR 5HT-1A OR 5HT-2B)

=> D 1-14 IBIB ABS

L15 ANSWER 1 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2005342126 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15992090
TITLE: Risperidone (Risperdal): clinical experience with a new antipsychosis drug.
AUTHOR: Keks N A; Culhane C
CORPORATE SOURCE: Monash University, Mental Health Research Institute of Victoria, Alfred Hospital, Prahran 3181, Australia.. N.Keks@alfred.org.au
SOURCE: Expert opinion on investigational drugs, (1999 Apr) Vol. 8, No. 4, pp. 443-52.
Journal code: 9434197. E-ISSN: 1744-7658.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; PUBMED-NOT-MEDLINE
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 6 Jul 2005
Last Updated on STN: 22 Jul 2005
Entered Medline: 21 Jul 2005

AB Risperidone (Risperdal) is a benzisoxazole derivative with a high affinity for serotonin 5-HT2 and dopamine D2 receptors, and some affinity for alpha- adrenergic, histamine H1 and dopamine D1 receptors. It has no anticholinergic effects. Early studies demonstrated risperidone to be an effective medication for psychotic symptoms, probably more so than the older neuroleptics for both positive and negative symptoms. At clinically effective doses, risperidone causes no more extrapyramidal side-effects (EPS) than placebo; at higher doses EPS frequency increases in a dose-dependent manner. Since it became available in 1994, extensive experience with the drug supports favourable early impressions of efficacy and tolerability. Minimal sedation, relatively little weight gain and absence of anticholinergic manifestations contribute to the relative tolerability of risperidone as compared to older neuroleptics. However, risperidone is associated with hyperprolactinaemia which can result in amenorrhoea and sexual dysfunction. Compared to older neuroleptics, pharmacoeconomic studies have shown that use of risperidone is associated with reduced hospitalisation and direct cost savings. A recent study found equivalent efficacy between risperidone and clozapine for treatment-resistant patients. Two studies comparing risperidone and olanzapine have yielded positive but conflicting findings. The overall positive experience with risperidone has resulted in the drug being widely recommended as a first line treatment option for psychoses.

L15 ANSWER 2 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2001036398 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10939309
TITLE: Risperidone: a review of its use in the management of the behavioural and psychological symptoms of dementia.
AUTHOR: Bhana N; Spencer C M
CORPORATE SOURCE: Adis International Limited, Mairangi Bay, Auckland, New Zealand.. demail@adis.co.nz
SOURCE: Drugs & aging, (2000 Jun) Vol. 16, No. 6, pp. 451-71. Ref: 74
Journal code: 9102074. ISSN: 1170-229X.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 30 Nov 2000

AB Risperidone is a benzisoxazole derivative which has proven efficacy against the positive and negative symptoms of schizophrenia. It has more recently been investigated and shown efficacy as a treatment for the behavioural and psychological symptoms associated with dementia in the elderly. Risperidone has pharmacological properties resembling those of the atypical antipsychotic clozapine and an improved tolerability profile compared with the conventional antipsychotic haloperidol. Risperidone has antagonistic activity primarily at serotonin 5-HT2A and dopamine D2 receptors. In the first 2 large, well controlled trials of an antipsychotic agent used in the treatment of elderly patients with Alzheimer's dementia, vascular dementia or mixed dementia, risperidone 1 mg/day was at least as effective as haloperidol and superior to placebo, as assessed by the rating scales for global behaviour, aggression and psychosis. In extension phases of the 2 trials, clinical benefits were maintained for treatment periods of up to 1 year, with an incidence rate of tardive dyskinesia (2.6%) one-tenth of that seen with conventional antipsychotics. Risperidone, administered at a low dosage of 1 mg/day was associated with fewer extrapyramidal symptoms compared with haloperidol in elderly patients. Risperidone was well tolerated with no clinically relevant abnormalities in laboratory tests, vital signs or electrocardiogram results. Conclusion: The efficacy of risperidone has been demonstrated in the treatment of the behavioural and psychological symptoms associated with dementia in the elderly. Preliminary results from 1-year extension studies confirm the favourable efficacy and tolerability profile of risperidone 1 mg/day. Although head to head studies with other atypical antipsychotic agents are required and the long term use of the drug requires clarification, risperidone represents a generally well tolerated and effective treatment in the management of dementia-associated behavioural and psychological symptoms in the elderly.

L15 ANSWER 3 OF 14 MEDLINE on STN

ACCESSION NUMBER: 1999187310 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10087034
TITLE: S-16924, a novel, potential antipsychotic with marked serotoninlA agonist properties. IV. A drug discrimination comparison with clozapine.
AUTHOR: Millan M J; Schreiber R; Monneyron S; Denorme B; Melon C; Queriaux S; Dekeyne A
CORPORATE SOURCE: Institut de Recherches Servier, Centre de Recherches de Croissy, Psychopharmacology Department, Croissy-sur-Seine, Paris, France.
SOURCE: The Journal of pharmacology and experimental therapeutics, (1999 Apr) Vol. 289, No. 1, pp. 427-36.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 4 May 1999
Last Updated on STN: 18 Jan 2003
Entered Medline: 21 Apr 1999

AB The novel benzodioxopyrrolidine (S-16924) displays a clozapine-like profile of interaction with multiple monoaminergic receptors, in addition to potent agonist activity at serotonin (5-HT)1A receptors. S-16924 (2.5 mg/kg i.p.) and clozapine (5.0 mg/kg i.p.) generated robust discriminative stimuli (DS) and displayed full mutual generalization. The D4 antagonists L-745,870 and S-18126, the D1/D5 antagonist SCH-39166, and the D3 antagonist S-14297 showed at most partial generalization to S-16924 and clozapine. The D2/D3 antagonist raclopride fully generalized to S-16924, but only partially generalized to clozapine. The 5-HT2A antagonist MDL-100, 907 fully generalized to S-16924 and two further 5-HT2A antagonists, fananserin and SR-46349, showed partial generalization. However, MDL-100,907, fananserin, and SR-46349 showed less pronounced generalization to clozapine. Similarly, the 5-HT2C antagonists SB-200,646 and SB-206,553 more markedly generalized to S-16924 than to clozapine. The 5-HT1A receptor agonist (+/-)-8-dihydroxy-2-(di-n-propylamino) tetralin generalized fully to S-16924 but not to clozapine. Full generalization was obtained to both S-16924 and clozapine for the clozapine congeners, olanzapine and quetiapine. In distinction, the benzisoxazole, risperidone, and the phenylindole, sertindole, weakly generalized to S-16924 and clozapine. However, the benzisoxazole ziprasidone, which possesses 5-HT1A agonist properties, generalized fully to S-16924 but not to clozapine. Finally, the muscarinic antagonist scopolamine generalized fully to clozapine and partially to S-16924. In conclusion, S-16924 and clozapine display both communalities and differences in their "compound" DS; this likely reflects their respective complex patterns of interaction with multiple monoaminergic receptors. Although no specific receptor was identified as underlying the clozapine DS, 5-HT1A agonist as well as D2 and 5-HT2A/2C antagonist properties contribute to the S-16924 DS.

L15 ANSWER 4 OF 14 MEDLINE on STN
ACCESSION NUMBER: 97308342 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9165568
TITLE: Neuroleptic malignant syndrome with risperidone.
AUTHOR: Gleason P P; Conigliaro R L
CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of Pharmacy, University of Pittsburgh, Pennsylvania, USA.
SOURCE: Pharmacotherapy, (1997 May-Jun) Vol. 17, No. 3, pp. 617-21.
Journal code: 8111305. ISSN: 0277-0008.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 24 Jul 1997
Last Updated on STN: 24 Jul 1997
Entered Medline: 15 Jul 1997

AB Neuroleptic malignant syndrome is thought to be a result of dopamine D2 receptor blockade in the striatum of the basal ganglia. Risperidone, a benzisoxazole derivative antipsychotic, has high serotonin 5-HT2 receptor blockade and dose-related D2 receptor blockade. The high ratio is believed to impart the low frequency of extrapyramidal symptoms with risperidone at low dosages. With this low frequency of extrapyramidal symptoms, it was thought the frequency of neuroleptic malignant syndrome might also be lowered. A 73-year-old woman developed neuroleptic malignant syndrome after monotherapy with risperidone. The syndrome reversed after discontinuing risperidone and starting treatment with dantrolene and bromocriptine. It appears that the protection from extrapyramidal side effects observed with risperidone does not ensure protection from neuroleptic malignant syndrome.

L15 ANSWER 5 OF 14 MEDLINE on STN
ACCESSION NUMBER: 96142226 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8543544
TITLE: Risperidone as a treatment for Tourette's syndrome.
AUTHOR: Bruun R D; Budman C L
CORPORATE SOURCE: Cornell University Medical School, New York, N.Y., USA.
SOURCE: The Journal of clinical psychiatry, (1996 Jan) Vol. 57, No. 1, pp. 29-31.
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 27 Feb 1996
Last Updated on STN: 27 Feb 1996
Entered Medline: 9 Feb 1996

AB BACKGROUND: An open-label trial was performed to assess the efficacy and safety of risperidone, a benzisoxazole derivative with potent D2 and 5-HT2 antagonism, for treatment of Tourette's syndrome. METHOD: Thirty-eight patients with Tourette's syndrome volunteered to take risperidone for treatment of their tics. All patients had failed to respond adequately to conventional treatments (with neuroleptics such as haloperidol and/or with the alpha 2-adrenergic agonist clonidine) or had suffered from intolerable side effects from such treatments. Patients were rated for tic severity by the Yale Global Tic Severity Scale (YGTSS) before treatment and after 1 month of treatment with risperidone. Patients were monitored carefully for side effects and clinical response. RESULTS: Of the 38 patients, 8 discontinued risperidone treatment before the end of the trial because of intolerable side effects. At the end of the 4-week trial, 22 patients (58%) were improved, 7 patients (18%) had no appreciable change in their symptoms, and 1 patient (3%) had a documented worsening of tics. Doses of risperidone at the end of the trial ranged from 0.5 mg to 9 mg/day (mean = 2.7 mg/day). CONCLUSION: This open clinical trial suggests that risperidone may be a promising alternative to conventional medications used for treating the symptoms of Tourette's syndrome.

L15 ANSWER 6 OF 14 MEDLINE on STN
ACCESSION NUMBER: 95348446 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7542676
TITLE: A pharmacological, pharmacokinetic and clinical overview of risperidone, a new antipsychotic that blocks serotonin 5-HT2 and dopamine D2 receptors.
AUTHOR: He H; Richardson J S

CORPORATE SOURCE: College of Pharmacy, College of Medicine, University of Saskatchewan, Saskatoon, Canada.
SOURCE: International clinical psychopharmacology, (1995 Mar) Vol. 10, No. 1, pp. 19-30. Ref: 78
Journal code: 8609061. ISSN: 0268-1315.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 11 Sep 1995
Last Updated on STN: 29 Jan 1996
Entered Medline: 30 Aug 1995

AB Risperidone is a benzisoxazole derivative with antipsychotic activity that is chemically unrelated to other currently available antipsychotic agents. Its neuropharmacological properties, characterized by potent central antagonism of both serotonin 5-HT2 and dopamine D2 receptors, also differ from those of most other antipsychotic drugs. The pharmacokinetics of risperidone are well understood, having been studied in healthy subjects as well as in psychotic patients. The absolute oral bioavailability of risperidone is nearly 70%, and after oral administration, it is rapidly absorbed with the plasma level reaching a peak at about 1 h. 9-Hydroxyrisperidone, one of the metabolites of risperidone, is equally active with the parent compound and so the clinical activity of a dose of risperidone is due to the combined actions of both moieties. The plasma concentrations of risperidone and its active metabolite remain dose proportional even at doses exceeding the therapeutic range. In clinical trials with chronic schizophrenia patients, risperidone has an overall therapeutic activity comparable with that of haloperidol, but at doses that produce similar improvements in the positive symptoms of schizophrenia, risperidone has a greater effect on the negative symptoms and produces less extrapyramidal side effects than does haloperidol. However, additional controlled clinical studies are needed before the claims that risperidone is therapeutically superior to haloperidol can be considered to be established firmly. Although risperidone is effective in acute schizophrenia and in non-treatment-resistant schizophrenics, studies adequately comparing risperidone with clozapine in treatment-resistant schizophrenic patients remain to be published. In addition, risperidone has been reported to be of value in patients with schizodepressive disorders. The clinical success of risperidone suggests that the development of compounds with selective affinity for 5-HT2 or other serotonin receptors may result in even further improvements in the pharmacotherapy of psychiatric disorders.

L15 ANSWER 7 OF 14 MEDLINE on STN
ACCESSION NUMBER: 95222523 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7707315
TITLE: 3-[[(Aryloxy)alkyl]piperidinyl]-1,2-benzisoxazoles as D2/5-HT2 antagonists with potential atypical antipsychotic activity: antipsychotic profile of iloperidone (HP 873).
AUTHOR: Strupczewski J T; Bordeau K J; Chiang Y; Glamkowski E J; Conway P G; Corbett R; Hartman H B; Szewczak M R; Wilmot C A; Helsley G C
CORPORATE SOURCE: Chemical Research Department, Hoechst-Roussel Pharmaceuticals Inc, Somerville, New Jersey 08876, USA.
SOURCE: Journal of medicinal chemistry, (1995 Mar 31) Vol. 38, No. 7, pp. 1119-31.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 18 May 1995
Last Updated on STN: 18 May 1995
Entered Medline: 11 May 1995

AB A series of 3-[[(aryloxy)alkyl]piperidinyl]-1,2-benzisoxazoles was synthesized and evaluated as potential antipsychotic D2/5-HT2 antagonists. Most of these compounds showed potent antipsychotic-like activity in an apomorphine-induced climbing mouse paradigm, with many also showing preferential mesolimbic activity, as indicated by their weaker effects in an apomorphine-induced stereotypy model. In receptor binding assays, many displayed a moderate affinity for the D2 receptor coupled with a significantly greater affinity for the 5-HT2 receptor: a property that has been suggested as necessary for atypicality. From this series, compound 45, 1-[4-[3-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1- piperidinyl]propoxy]-3-methoxyphenyl]ethanone (iloperidone, HP 873), was further evaluated in a battery of in vivo and in vitro assays. This compound showed a 300-fold greater potency in inhibition of climbing than in inhibition of stereotypy or induction of catalepsy, and when evaluated chronically in an electrophysiological model, 45 caused a depolarization blockade of dopamine neurons in the A10 area of the rat brain but not in the A9 area. Additionally, it showed positive activity in a social interaction paradigm, suggesting potential efficacy against asociality, a component of the negative symptoms of schizophrenia. In chronic ex vivo studies, 45, similar to clozapine, caused a down regulation of 5-HT2 receptors but had no effect on the number of D2 receptors. Compound 45 is currently undergoing clinical evaluation.

L15 ANSWER 8 OF 14 MEDLINE on STN
ACCESSION NUMBER: 95148787 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7531352
TITLE: Regional brain distribution of risperidone and its active metabolite 9-hydroxy-risperidone in the rat.
AUTHOR: van Beijsterveldt L E; Geerts R J; Leysen J E; Megens A A; Van den Eynde H M; Meuldermans W E; Heykants J J
CORPORATE SOURCE: Department of Drug Metabolism and Pharmacokinetics, Janssen Research Foundation, Beerse, Belgium.
SOURCE: Psychopharmacology, (1994 Feb) Vol. 114, No. 1, pp. 53-62.
Journal code: 7608025. ISSN: 0033-3158.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 16 Mar 1995
Last Updated on STN: 29 Jan 1996
Entered Medline: 8 Mar 1995

AB Risperidone is a new benzisoxazole antipsychotic. 9-Hydroxy-risperidone is the major plasma metabolite of risperidone. The pharmacological properties of 9-hydroxy-risperidone were studied and appeared to be comparable to those of risperidone itself, both in respect of the profile of interactions with various neurotransmitters and its potency, activity, and onset and duration of action. The absorption, plasma levels and regional brain distribution of risperidone, metabolically formed 9-hydroxy-risperidone and total radioactivity were studied in the male Wistar rat after single subcutaneous administration of radiolabelled risperidone at 0.02 mg/kg. Concentrations were determined by HPLC separation, and off-line determination of the radioactivity with liquid scintillation counting. Risperidone was well absorbed. Maximum plasma concentrations were reached at 0.5-1 h after subcutaneous administration. Plasma concentrations of 9-hydroxy-risperidone were higher than those of risperidone from 2h after dosing. In plasma, the apparent elimination half-life of risperidone was 1.0 h, and mean residence times were 1.5 h for risperidone and 2.5 h for its 9-hydroxy metabolite. Plasma levels of the radioactivity increased dose

proportionally between 0.02 and 1.3 mg/kg. Risperidone was rapidly distributed to brain tissues. The elimination of the radioactivity from the frontal cortex and striatum--brain regions with high concentrations of 5-HT2 or dopamine-D2 receptors--became more gradual with decreasing dose levels. After a subcutaneous dose of 0.02 mg/kg, the ED50 for central 5-HT2 antagonism in male rats, half-lives in frontal cortex and striatum were 3-4 h for risperidone, whereas mean residence times were 4-6 h for risperidone and about 12 h for 9-hydroxy-risperidone. These half-lives and mean residence times were 3-5 times longer than in plasma and in cerebellum, a region with very low concentrations of 5-HT2 and D2 receptors. Frontal cortex and striatum to plasma concentration ratios increased during the experiment. The distribution of 9-hydroxy-risperidone to the different brain regions, including frontal cortex and striatum, was more limited than that of risperidone itself. This indicated that 9-hydroxy-risperidone contributes to the in vivo activity of risperidone, but to a smaller extent than would be predicted from plasma levels. AUCs of both active compounds in frontal cortex and striatum were 10-18 times higher than those in cerebellum. No retention of metabolites other than 9-hydroxy-risperidone was observed in any of the brain regions investigated.

L15 ANSWER 9 OF 14 MEDLINE on STN
ACCESSION NUMBER: 95023318 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7524043
TITLE: Risperidone.
AUTHOR: Cohen L J
CORPORATE SOURCE: College of Pharmacy, University of Oklahoma, Oklahoma City 73190.
SOURCE: Pharmacotherapy, (1994 May-Jun) Vol. 14, No. 3, pp. 253-65. Ref: 62
Journal code: 8111305. ISSN: 0277-0008.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 22 Dec 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 21 Nov 1994

AB Risperidone, a benzisoxazole derivative, is a novel antipsychotic agent that has an extremely strong binding affinity for serotonin 5-HT2 receptors, a strong binding affinity for dopamine D2 receptors, and a high affinity for alpha 1- and alpha 2-adrenergic receptors and histamine H1 receptors. Its affinity for serotonin receptors is approximately 200 times greater than that of haloperidol, and its dopamine antagonistic potency is comparable to that of haloperidol. Its major metabolite, 9-hydroxyrisperidone, has similar pharmacologic activity, and thus the parent compound and metabolite form the active antipsychotic moiety. Clinical trials demonstrate that risperidone is an effective antipsychotic agent that improves negative as well as positive symptoms of schizophrenia. At recommended dosages, the frequency of extrapyramidal side effects is no greater than that seen with placebo. The drug appears to be an advance in the treatment of psychoses.

L15 ANSWER 10 OF 14 MEDLINE on STN
ACCESSION NUMBER: 94334885 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7914536
TITLE: Benzisoxazole- and benzisothiazole-3-carboxamides as potential atypical antipsychotic agents.
AUTHOR: Hrib N J; Jurcak J G; Burgher K L; Conway P G; Hartman H B; Kerman L L; Roehr J E; Woods A T
CORPORATE SOURCE: Neuroscience Strategic Business Unit, Hoechst-Roussel Pharmaceuticals, Inc., Somerville, New Jersey 08876.
SOURCE: Journal of medicinal chemistry, (1994 Jul 22) Vol. 37, No. 15, pp. 2308-14.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 20 Sep 1994
Last Updated on STN: 6 Feb 1995
Entered Medline: 12 Sep 1994

AB A series of benzisoxazole- and benzisothiazole-3-carboxamides has been prepared and tested for potential antipsychotic activity. In general, the compounds showed an affinity for dopamine D2 and serotonin 5HT2A and 5HT1A receptors. Several members of this series have demonstrated activity in animal models predictive of potential antipsychotic activity. In addition, compounds 18, 19, 22, 27, 28, 43, and 44 have also shown a potential for reduced EPS liability as suggested by the ratio of activity seen in mesolimbic-mediated vs nigrostriatal-mediated behavioral assays.

L15 ANSWER 11 OF 14 MEDLINE on STN
ACCESSION NUMBER: 94046936 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7901415
TITLE: Examination of the D2/5-HT2 affinity ratios of resolved 5,6,7,8,9,10-hexahydro-7,10-iminocyclohept[b]indoles: an enantioselective approach toward the design of potential atypical antipsychotics.
AUTHOR: Mewshaw R E; Abreu M E; Silverman L S; Mathew R M; Tiffany C W; Bailey M A; Karbon E W; Ferkany J W; Kaiser C
CORPORATE SOURCE: Department of Medicinal Chemistry, Scios Nova Inc., Baltimore, Maryland 21224-6522.
SOURCE: Journal of medicinal chemistry, (1993 Oct 15) Vol. 36, No. 21, pp. 3073-6.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 17 Jan 1994
Last Updated on STN: 3 Feb 1997
Entered Medline: 26 Nov 1993

AB Enantiomers of several N-substituted 5,6,7,8,9,10-hexahydro-7,10-iminocyclohept[b]indoles were obtained by the resolution of 2-fluoro-5,6,7,8,9,10-hexahydro-7,10-iminocyclohept[b]indole and 5,6,7,8,9,10-hexahydro-7,10-iminocyclohept[b]indole followed by N-alkylation. These, as well as the racemates, were evaluated for their affinity for the 5-HT2 and D2 receptors. Those compounds possessing the 7S,10R stereochemistry were consistently recognized by the 5-HT2 and D2 receptors as the eutomer. 2-Fluoro-11-[4-(4-fluorophenyl)-4-oxobutyl]-5,6,7,8,9,10-hexahydro-7S,10 R-iminocyclohept[b]indole [(7S,10R)-8] had the highest affinity for the 5-HT2 receptor (Ki = 0.80 nM), while its distomer (7R,10S)-8 was the most selective member of this class of bridged gamma-carbolines (D2 /5-HT2 = 562). Incorporation of a benzoyl or isosteric benzisoxazole moiety tethered by a four-carbon spacer to a bridged gamma-carboline nucleus, possessing the 7S,10R absolute configuration, produced high affinity ligands for the 5-HT2 and D2 receptors.

L15 ANSWER 12 OF 14 MEDLINE on STN
ACCESSION NUMBER: 93267591 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8496917
TITLE: Bridged gamma-carbolines and derivatives possessing selective and combined affinity for 5-HT2 and D2

receptors.

AUTHOR: Mewshaw R E; Silverman L S; Mathew R M; Kaiser C; Sherrill R G; Cheng M; Tiffany C W; Karbon E W; Bailey M A; Borosky S A; +

CORPORATE SOURCE: Scios Nova Inc., Baltimore, Maryland 21224-6522.

SOURCE: Journal of medicinal chemistry, (1993 May 14) Vol. 36, No. 10, pp. 1488-95.
Journal code: 9716531. ISSN: 0022-2623.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199306

ENTRY DATE: Entered STN: 2 Jul 1993
Last Updated on STN: 2 Jul 1993
Entered Medline: 22 Jun 1993

AB A series of 5,6,7,8,9,10-hexahydro-7,10-iminocyclohept[b]indoles and 6,7,8,9,10,11-hexahydro-7,11-imino-5H-cyclooct[b]indoles was prepared. Structural modifications of the lead compound, 11-[4-(4-fluorobenzoyl)propyl]-5,6,7,8,9,10-hexahydro-7,10- iminocyclohept[b]indole (5, Ki = 0.82 nM vs [3H]ketanserin) enabled the identification of the functionality necessary for high affinity at serotonin 5-HT2 and dopamine D2 receptors in ligand binding studies. The indole ring, as well as the benzoyl or isosteric benzisoxazole moiety, were essential for high affinity. Variations of the length of the side chains resulted in ligands having either selective affinity for the 5-HT2 receptor or a combination of 5-HT2 and D2 affinity. In vivo binding studies were performed on selected members in this series. The most potent member, 2-fluoro-11-[4-(4-fluorobenzoyl)butyl]-5,6,7,8,9,10-hexahydro-7,10-iminocyclohept[b]indole (36) had an ED50 of < 1 mg/kg at the 5-HT2 and D2 receptors following oral administration.

L15 ANSWER 13 OF 14 MEDLINE on STN

ACCESSION NUMBER: 91157658 MEDLINE

DOCUMENT NUMBER: PubMed ID: 2127339

TITLE: [Development of new antipsychotic drugs].
El desarrollo de nuevas drogas antipsicoticas.

AUTHOR: Vanden Bussche G; Gelders Y G; Heylen S L

CORPORATE SOURCE: Clinical Research and Development Department, Janssen Research Foundation, Beerse, Belgica.

SOURCE: Acta psiquiatrica y psicologica de America latina, (1990 Jan-Jun) Vol. 36, No. 1-2, pp. 13-25.
Journal code: 0373060. ISSN: 0001-6896.

PUB. COUNTRY: Argentina

DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Spanish

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199104

ENTRY DATE: Entered STN: 28 Apr 1991
Last Updated on STN: 28 Apr 1991
Entered Medline: 8 Apr 1991

AB As far as schizophrenia is concerned, therapeutical effects of neuroleptics based on brain-located dopamine receptor blockers are taken for granted. It is also admitted, however, that classical neuroleptics have inconveniences, namely: Their relative lack of effect on negative symptoms, and their liability to induce extrapyramidal symptoms (EPS). Pipamperone-based clinical studies evidenced that an antagonist combining serotonin 5-HT2, and dopamine D2 was successful in the treatment of schizophrenia--which could be clearly observed in (a) anti-autistic effects, (b) regulating disrupted sleep-wake rhythms, and (c) a lesser tendency to EPS. Setoperone-based studies--a compound with a comparable pharmacological profile--confirmed the above observations. Until, however, the synthesis of ritanserin--a specific, and selective antagonistic receptor--was not achieved, no exact implication of 5-HT2 antagonist in psychopharmacological treatments of schizophrenia could be explored further. Indeed, double-blind trials evidenced a remarkable improvement in negative as well as extrapyramidal symptoms. Since a monotherapy appeared as undeniably called for in the treatment of schizophrenia, the next logical step to be taken was selecting a compound with a central antagonism comparable to ritanserin's, and a central D2 antagonism comparable to haloperidol's. Among a chemical range of benzisoxazole derivatives, risperidone was thus selected. The first double-blind trials on chronic schizophrenic patients seem indeed to confirm that this substance is likely to get over the above mentioned inconveniences, so typical of classical neuroleptics.

L15 ANSWER 14 OF 14 MEDLINE on STN

ACCESSION NUMBER: 88155393 MEDLINE

DOCUMENT NUMBER: PubMed ID: 2450200

TITLE: Pharmacology of risperidone (R 64 766), a new antipsychotic with serotonin-S2 and dopamine-D2 antagonistic properties.

AUTHOR: Janssen P A; Niemegeers C J; Awouters F; Schellekens K H; Megens A A; Meert T F

CORPORATE SOURCE: Department of Pharmacology, Janssen Research Foundation, Beerse, Belgium.

SOURCE: The Journal of pharmacology and experimental therapeutics, (1988 Feb) Vol. 244, No. 2, pp. 685-93.
Journal code: 0376362. ISSN: 0022-3565.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198804

ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 12 Apr 1988

AB Comparative studies of the benzisoxazole derivative risperidone (R 64 766) were made with ritanserin, a selective centrally acting serotonin-S2 antagonist and with haloperidol, a selective centrally acting dopamine-D2 antagonist. Risperidone like ritanserin shows activity in all tests related to serotonin-S2 antagonism, but at even lower doses (peripheral S2-antagonism at 0.0011 mg/kg, central S2-antagonism at 0.014 mg/kg). Like haloperidol, risperidone shows activity in all tests related to dopamine-D2 antagonism; activity in rats for both compounds starts at 0.016 mg/kg, but some central nervous system controlled functions, including the induction of catalepsy, are relatively much less affected by risperidone. Qualitatively, risperidone is a mixed serotonin-dopamine antagonist. Quantitatively, its study in dogs reveals potent dopamine-D2 antagonistic activity with excellent p.o. bioavailability and a relatively long duration of action. From the obtained pharmacological data, risperidone could be expected to possess the complementary clinical effects of a ritanserin-like serotonin-S2 and an haloperidol-like dopamine-D2 antagonist. Serotonin-S2 antagonism may improve the quality of sleep, reduce negative and affective symptoms in schizophrenic patients and decrease extrapyramidal symptoms induced by classical neuroleptics. Because risperidone is a dopamine-D2 antagonist, antidelusional, antihallucinatory and antimanic actions are expected. The first clinical studies indicate that two additional therapeutic targets, which are not reached with classical neuroleptics, may be obtained with risperidone in the monotherapy of schizophrenia and related disorders: very important contact and mood-elevating properties and extrapyramidal symptoms-free maintenance therapy.

=>

---Logging off of STN---

```
=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              16.41      47.87

STN INTERNATIONAL LOGOFF AT 13:24:47 ON 09 APR 2007


Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:ssspta1623zct

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  DEC 18  CA/CAplus pre-1967 chemical substance index entries enhanced
                  with preparation role
 NEWS  4  DEC 18  CA/CAplus patent kind codes updated
 NEWS  5  DEC 18  MARPAT to CA/CAplus accession number crossover limit increased
                  to 50,000
 NEWS  6  DEC 18  MEDLINE updated in preparation for 2007 reload
 NEWS  7  DEC 27  CA/CAplus enhanced with more pre-1907 records
 NEWS  8  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS  9  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS 10  JAN 16  IPC version 2007.01 thesaurus available on STN
 NEWS 11  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS 12  JAN 22  CA/CAplus updated with revised CAS roles
 NEWS 13  JAN 22  CA/CAplus enhanced with patent applications from India
 NEWS 14  JAN 29  PHAR reloaded with new search and display fields
 NEWS 15  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 16  FEB 15  PATDPASPC enhanced with Drug Approval numbers
 NEWS 17  FEB 15  RUSSIAPAT enhanced with pre-1994 records
 NEWS 18  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 19  FEB 26  MEDLINE reloaded with enhancements
 NEWS 20  FEB 26  EMBASE enhanced with Clinical Trial Number field
 NEWS 21  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
 NEWS 22  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 23  FEB 26  CAS Registry Number crossover limit increased from 10,000
                  to 300,000 in multiple databases
 NEWS 24  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 25  MAR 16  CASREACT coverage extended
 NEWS 26  MAR 20  MARPAT now updated daily
 NEWS 27  MAR 22  LWPI reloaded
 NEWS 28  MAR 30  RDISCLOSURE reloaded with enhancements
 NEWS 29  MAR 30  INPADOCDB will replace INPADOC on STN
 NEWS 30  APR 02  JICST-EPLUS removed from database clusters and STN

 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:55:13 ON 09 APR 2007

=> file medline
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               0.21       0.21

FILE 'MEDLINE' ENTERED AT 13:55:53 ON 09 APR 2007

 FILE LAST UPDATED: 7 Apr 2007 (20070407/UP).  FILE COVERS 1950 TO DATE.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s 5htlb or 5-htlb or 5ht-lbh
          137 5HTLB
      2352638 5
         1858 HTLB
         1855 5-HTLB
                (5(W)HTLB)
         2604 5HT
            2 LBH
            0 5HT-LBH
                (5HT(W)LBH)
L1       1953 5HTLB OR 5-HTLB OR 5HT-LBH

=> s 5htlb or 5-htlb or 5ht-lb
          137 5HTLB
      2352638 5
         1858 HTLB
         1855 5-HTLB
                (5(W)HTLB)
         2604 5HT
        13798 LB
           55 5HT-LB
                (5HT(W)LB)
L2       1984 5HTLB OR 5-HTLB OR 5HT-LB

=> s l2 and antagon?
       575230 ANTAGON?
L3       1099 L2 AND ANTAGON?

=> s l3 and new
```

```
       1000180 NEW
          5806 NEWS
       1005218 NEW
                  (NEW OR NEWS)
L4          67 L3 AND NEW

=> s l4 and 2003/py
        569314 2003/PY
                  (20030000-20039999/PY)
L5           4 L4 AND 2003/PY

=> d 1-4 ibib abs

L5   ANSWER 1 OF 4     MEDLINE on STN
ACCESSION NUMBER:   2004418030     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15320857
TITLE:              Migraine: pathophysiology, pharmacology, treatment and
                    future trends.
AUTHOR:             Villalon Carlos M; Centurion David; Valdivia Luis Felipe;
                    de Vries Peter; Saxena Pramod R
CORPORATE SOURCE:   Departamento de Farmacobiologia, CINVESTAV-IPN, Czda. de
                    los Tenorios 235, Col. Granjas Coapa, Deleg. Tlalpan, CP
                    14330, Mexico DF, Mexico.. carlos_villalon@infosel.net.mx
SOURCE:             Current vascular pharmacology, (2003 Mar) Vol. 1,
                    No. 1, pp. 71-84.  Ref: 110
                    Journal code: 101157208. ISSN: 1570-1611.
PUB. COUNTRY:       United Arab Emirates
DOCUMENT TYPE:      Historical
                    Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200412
ENTRY DATE:         Entered STN: 25 Aug 2004
                    Last Updated on STN: 19 Dec 2004
                    Entered Medline: 1 Dec 2004
AB  Migraine treatment has evolved into the scientific arena, but it seems
    still controversial whether migraine is primarily a vascular or a
    neurological dysfunction.  Irrespective of this controversy, the levels of
    serotonin (5-hydroxytryptamine; 5-HT), a vasoconstrictor and a central
    neurotransmitter, seem to decrease during migraine (with associated
    carotid vasodilatation) whereas an i.v. infusion of 5-HT can abort
    migraine.  In fact, 5-HT as well as ergotamine, dihydroergotamine and
    other antimigraine agents invariably produce vasoconstriction in the
    external carotid circulation.  The last decade has witnessed the advent of
    sumatriptan and second generation triptans (e.g. zolmitriptan,
    rizatriptan, naratriptan), which belong to a new class of drugs,
    the 5-HT1B/1D/1F receptor agonists.  Compared to
    sumatriptan, the second-generation triptans have a higher oral
    bioavailability and longer plasma half-life.  In line with the vascular
    and neurogenic theories of migraine, all triptans produce selective
    carotid vasoconstriction (via 5-HT1B receptors) and
    presynaptic inhibition of the trigeminovascular inflammatory responses
    implicated in migraine (via 5-HT1D/5-ht1F receptors).  Moreover, selective
    agonists at 5-HT1D (PNU-142633) and 5-ht1F (LY344864) receptors inhibit
    the trigeminovascular system without producing vasoconstriction.
    Nevertheless, PNU-142633 proved to be ineffective in the acute treatment
    of migraine, whilst LY344864 did show some efficacy when used in doses
    which interact with 5-HT1B receptors.  Finally,
    although the triptans are effective antimigraine agents producing
    selective cranial vasoconstriction, efforts are being made to develop
    other effective antimigraine alternatives acting via the direct blockade
    of vasodilator mechanisms (e.g. antagonists at CGRP receptors,
    antagonists at 5-HT7 receptors, inhibitors of nitric oxide
    biosynthesis, etc).  These alternatives will hopefully lead to fewer side
    effects.

L5   ANSWER 2 OF 4     MEDLINE on STN
ACCESSION NUMBER:   2003200109     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12644890
TITLE:              Role of extracellular serotonin levels in the effect of
                    5-HT1B receptor blockade.
AUTHOR:             de Groote Lotte; Klompmakers Andre A; Olivier Berend;
                    Westenberg Herman G M
CORPORATE SOURCE:   Department of Psychiatry, Rudolf Magnus Institute of
                    Neuroscience, University Medical Center Utrecht,
                    Heidelberglaan 100, 3584 CX Utrecht, The Netherlands.
SOURCE:             Psychopharmacology, (2003 May) Vol. 167, No. 2,
                    pp. 153-8.  Electronic Publication: 2003-03-18.
                    Journal code: 7608025. ISSN: 0033-3158.
PUB. COUNTRY:       Germany: Germany, Federal Republic of
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200310
ENTRY DATE:         Entered STN: 30 Apr 2003
                    Last Updated on STN: 15 Oct 2003
                    Entered Medline: 14 Oct 2003
AB  The release of serotonin (5-HT) at serotonergic nerve terminals is
    regulated by 5-HT(1B) autoreceptors.  Several studies have reported that
    the effects of selective 5-HT reuptake inhibitors (SSRIs) on extracellular
    5-HT are augmented by 5-HT(1B) receptor antagonists, whereas
    administration of these antagonists alone do not enhance 5-HT
    levels.  It has been suggested that 5-HT(1B) receptors have low basal
    endogenous activity and therefore elevated endogenous 5-HT levels are
    needed to elicit an effect of 5-HT(1B) receptor antagonists.  To
    test this hypothesis, different strategies were used to enhance 5-HT
    levels in the rat frontal cortex to assess the effects of locally applied
    NAS-181, a new selective 5-HT(1B) receptor antagonist.
    Blockade of 5-HT(1B) receptors with NAS-181 dose dependently augmented
    5-HT levels when 5-HT levels were enhanced by a SSRI.  No additional
    effect of NAS-181 on 5-HT output was found when 5-HT levels were enhanced
    by KCl depolarization-induced release or by preventing degradation of 5-HT
    with the monoamine oxidase inhibitor pargyline.  In the presence of
    fluvoxamine, the increased 5-HT release evoked by KCl depolarization was
    augmented by NAS-181, supporting the idea that blockade of 5-HT
    transporters is necessary to measure an effect of 5-HT(1B) receptor
    blockade.  In conclusion, the results provide circumstantial evidence that
    the effect of a 5-HT(1B) receptor antagonist depends on
    extracellular 5-HT levels, but strongly suggest that additional 5-HT
    reuptake inhibition is required to detect any effect of 5-HT(1B) receptor
    antagonist on 5-HT levels by in vivo microdialysis.

L5   ANSWER 3 OF 4     MEDLINE on STN
ACCESSION NUMBER:   2003132987     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12595948
TITLE:              An evaluation of the effect of NAS-181, a new
                    selective 5-HT(1B) receptor antagonist, on
                    extracellular 5-HT levels in rat frontal cortex.
AUTHOR:             de Groote Lotte; Klompmakers Andre A; Olivier Berend;
                    Westenberg Herman G M
CORPORATE SOURCE:   Department of Psychiatry, Rudolf Magnus Institute of
                    Neuroscience, University Medical Center Utrecht,
                    Heidelberglaan 100, 3584 CX, Utrecht, The Netherlands.
SOURCE:             Naunyn-Schmiedeberg's archives of pharmacology, (2003
                    Feb) Vol. 367, No. 2, pp. 89-94.  Electronic
                    Publication: 2003-01-24.
                    Journal code: 0326264. ISSN: 0028-1298.
PUB. COUNTRY:       Germany: Germany, Federal Republic of
```

DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 22 Mar 2003
Last Updated on STN: 24 Dec 2003
Entered Medline: 23 Dec 2003

AB In the mammalian brain 5-HT(1B) receptors are present as autoreceptors regulating the release of serotonin (5-HT) by inhibitory feedback. The antagonistic properties of NAS-181 ((R)-(+)-2-{[[3-(Morpholinomethyl)-2H-chromen-8-yl]oxy]methyl} morpholine methane sulfonate), a new selective antagonist for the rodent 5-HT(1B) receptor, were determined by using an agonist-induced decrease of extracellular 5-HT. The 5-HT(1B) receptor agonist CP93129 (0.030.3 microM) applied by reversed microdialysis, dose-dependently reduced 5-HT levels in rat frontal cortex. The suppressant effect of CP93129 (0.1 microM) was smaller in the presence of fluvoxamine (3-10 microM), a 5-HT reuptake inhibitor. The effects of NAS-181 on CP93129 were compared with GR127935, a mixed 5-HT (1B/1D) receptor antagonist, and SB224289, a 5-HT(1B) receptor antagonist. Both in the presence and absence of fluvoxamine, the suppressant effect of CP93129 on extracellular 5-HT was attenuated by NAS-181 (1 microM) and GR127935 (10 microM), but not by SB224289 (1 microM). In the absence of fluvoxamine, GR127935, SB224289 and NAS-181 all reduced 5-HT levels, suggesting partial agonistic properties of these compounds. In conclusion, the results show that NAS-181 is a potent 5-HT(1B) receptor antagonist.

L5 ANSWER 4 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2003094519 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12606921
TITLE: The role of 5-HT1A/B autoreceptors in the antinociceptive effect of systemic administration of acetaminophen.
AUTHOR: Roca-Vinardell Aranzazu; Ortega-Alvaro Antonio; Gibert-Rahola Juan; Mico Juan A
CORPORATE SOURCE: Department of Neuroscience, Faculty of Medicine, University of Cadiz, Spain.
SOURCE: Anesthesiology, (2003 Mar) Vol. 98, No. 3, pp. 741-7.
Journal code: 1300217. ISSN: 0003-3022.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 28 Feb 2003
Last Updated on STN: 28 Mar 2003
Entered Medline: 27 Mar 2003

AB BACKGROUND: It has been proposed that serotonin participates in the central antinociceptive effect of acetaminophen. The serotonin activity in the brainstem is primarily under the control of 5-HT1A somatodendritic receptors, although some data also suggest the involvement of 5-HT1B receptors. In the presence of serotonin, the blockade of 5-HT(1A/B) receptors at the level of the raphe nuclei leads to an increase in serotonin release in terminal areas, thus improving serotonin functions. This study examines the involvement of 5-HT(1A/B) receptors in the antinociceptive effect of acetaminophen in mice. METHODS: The effects of acetaminophen (600 mg/kg intraperitoneal) followed by different doses of antagonists (WAY 100635 [0.2-0.8 mg/kg subcutaneous] and SB 216641 [0.2-0.8 mg/kg subcutaneous]) or agonists (8-OH-DPAT [0.25-1 mg/kg subcutaneous] and CP 93129 [0.125-0.5 mg/kg subcutaneous]) of 5-HT1A and 5-HT1B receptors, respectively, were determined in the hot-plate test in mice. RESULTS: Acetaminophen (300-800 mg/kg) showed a dose-dependent antinociceptive effect in the hot-plate test in mice. WAY 100635 (0.2-0.8 mg/kg; 5-HT1A antagonist) induced an increase in the antinociceptive effect of 600 mg/kg acetaminophen, but this increase was not dose related. Conversely, 8-OH-DPAT (0.25-1 mg/kg; 5-HT1A agonist) decreased the antinociceptive effect of acetaminophen. SB 216641 (0.2-0.8 mg/kg; 5-HT1B antagonist) induced a dose-related increase in the antinociceptive effect of acetaminophen, and CP 93129 (0.25 mg/kg; 5-HT1B agonist) significantly decreased the antinociceptive effect of acetaminophen. CONCLUSIONS: These results suggest that the combination of acetaminophen with compounds having 5-HT1A and 5-HT1B antagonist properties could be a new strategy to improve the analgesia of acetaminophen, thanks to its mild serotonergic properties.

```
=> s 2003 and d2 and (5ht1b or 5ht-1b or 5-ht1b) and (5ht2a or 5ht-2a or 5-ht2a)
        46652 2003
        26201 D2
          137 5HT1B
         2604 5HT
        13798 1B
           55 5HT-1B
                (5HT(W)1B)
      2352638 5
         1858 HT1B
         1855 5-HT1B
                (5(W)HT1B)
          179 5HT2A
         2604 5HT
        23242 2A
           78 5HT-2A
                (5HT(W)2A)
      2352638 5
         2592 HT2A
         2579 5-HT2A
                (5(W)HT2A)
L6           0 2003 AND D2 AND (5HT1B OR 5HT-1B OR 5-HT1B) AND (5HT2A OR 5HT-2A
               OR 5-HT2A)

=> s 2003/py and d2 and (5ht1b or 5ht-1b or 5-ht1b) and (5ht2a or 5ht-2a or 5-ht2a)
       569314 2003/PY
                (20030000-20039999/PY)
        26201 D2
          137 5HT1B
         2604 5HT
        13798 1B
           55 5HT-1B
                (5HT(W)1B)
      2352638 5
         1858 HT1B
         1855 5-HT1B
                (5(W)HT1B)
          179 5HT2A
         2604 5HT
        23242 2A
           78 5HT-2A
                (5HT(W)2A)
      2352638 5
         2592 HT2A
         2579 5-HT2A
                (5(W)HT2A)
L7           1 2003/PY AND D2 AND (5HT1B OR 5HT-1B OR 5-HT1B) AND (5HT2A OR
               5HT-2A OR 5-HT2A)

=> d
```

L7 ANSWER 1 OF 1 MEDLINE on STN
AN 2003157926 MEDLINE
DN PubMed ID: 12650952
TI Investigating the role of dopaminergic and serotonergic candidate genes in obsessive-compulsive disorder.
AU Hemmings Sian M J; Kinnear Craig J; Niehaus Dana J H; Moolman-Smook Johanna C; Lochner Christine; Knowles James A; Corfield Valerie A; Stein Dan J
CS MRC/US Centre for Molecular and Cellular Biology, University of Stellenbosch, P.O. Box 19063, 7505, Tygerberg, South Africa.. smjh@sun.ac.za
SO European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology, (2003 Mar) Vol. 13, No. 2, pp. 93-8. Journal code: 9111390. ISSN: 0924-977X.
CY Netherlands
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 6 Apr 2003
Last Updated on STN: 13 May 2003
Entered Medline: 12 May 2003

=> d abs

L7 ANSWER 1 OF 1 MEDLINE on STN
AB There is increasing evidence that the aetiology of obsessive-compulsive disorder (OCD) has a marked genetic component, although the precise mechanism of inheritance is unclear. Clinical and pharmacological studies have implicated the serotonergic and dopaminergic systems in disease pathogenesis. This study investigated the role of attractive candidate genes in the serotonergic and dopaminergic pathways in the development of OCD. The distribution of selected polymorphic variants in the serotonin receptor type 2A and 1Dbeta (5-HT(2A), 5-HT(1Dbeta)), dopamine transporter (DAT), dopamine receptor type 4 (DRD4) and monoamine-oxidase A (MAO-A) genes were analysed in 71 OCD cases and 129 control individuals in the genetically homogeneous Afrikaner population, by means of case-control association studies. Although no statistically significant genotypic or allelic associations were detected, the data yielded interesting preliminary results that warrant further discussion and investigation.

=> s d2 and (5ht1b or 5ht-1b or 5-ht1b) and (5ht2a or 5ht-2a or 5-ht2a)
26201 D2
137 5HT1B
2604 5HT
13798 1B
55 5HT-1B
(5HT(W)1B)
2352638 5
1858 HT1B
1855 5-HT1B
(5(W)HT1B)
179 5HT2A
2604 5HT
23242 2A
78 5HT-2A
(5HT(W)2A)
2352638 5
2592 HT2A
2579 5-HT2A
(5(W)HT2A)

L8 15 D2 AND (5HT1B OR 5HT-1B OR 5-HT1B) AND (5HT2A OR 5HT-2A OR 5-HT2A)

=> d 1-15 ibib abs hitstr
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'MEDLINE'

The following are valid formats:

The default display format is BIB.

ABS ---- AB
ALL ---- AN, DN, TI, AU, CS, NC, SO, CM, CY, DT, LA, FS, NCT, OS, EM, ED, AB, ST, CT, NA, RN, CN, GEN
BIB ---- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
CBIB --- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
DALL --- ALL, delimited for post processing
IABS --- ABS, with a text label
IALL --- ALL, indented with text labels
IBIB --- BIB, indented with text labels
IND ---- ST, CT, NA, RN, CN, GEN
TRIAL -- TI, ST, CT, NA, RN, CN, GEN (SAM, TRI, FREE)
HIT ---- All fields containing hit terms
HITIND - IND
KWIC --- All hit terms plus 20 words on either side
OCC ---- List of display fields containing hit terms

Hit terms will be highlighted in all available fields except CM and PY.

To display a particular field or fields, enter the display field codes. For a list of display field codes, enter 'HELP DFIELDS' at an arrow prompt (=>). Examples of formats include: 'BIB'; 'AB'; 'SO,ST'. You may specify the format fields in any order, and the information will be displayed in the same order as the format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be used with the DISPLAY ACC command to display the record for a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

=> d 1-15 ibib abs

L8 ANSWER 1 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2006514916 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16820177
TITLE: Quantitative mapping shows that serotonin rather than dopamine receptor mRNA expressions are affected after repeated intermittent administration of MDMA in rat brain.
AUTHOR: Kindlundh-Hogberg Anna M S; Svenningsson Per; Schioth Helgi B
CORPORATE SOURCE: Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden.. anna.kindlundh@neuro.uu.se
SOURCE: Neuropharmacology, (2006 Sep) Vol. 51, No. 4, pp. 838-47. Electronic Publication: 2006-07-03. Journal code: 0236217. ISSN: 0028-3908.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200611
ENTRY DATE: Entered STN: 30 Aug 2006

Last Updated on STN: 7 Nov 2006
Entered Medline: 6 Nov 2006

AB Ecstasy, (+/-)-3,4-methylenedioxy-metamphetamine (MDMA), is a popular recreational drug among young people. The present study aims to mimic MDMA intake among adolescents at dance clubs, taking repeated doses in the same evening on an intermittent basis. Male Sprague-Dawley rats received either 3x1 or 3x5 mg/kg/day (3 h apart) every seventh day during 4 weeks. We used real-time RT-PCR to determine the gene expression of serotonin 5HT1A, 5HT1B, 5HT2A, 5HT2C, 5HT3, 5HT6 receptors and dopamine D1, D2, D3 receptors in seven brain nuclei. The highest dose of MDMA extensively increased the 5HT1B-receptor mRNA in the cortex, caudate putamen, nucleus accumbens, and hypothalamus. The 5HT2A-receptor mRNA was reduced at the highest MDMA dose in the cortex. The 5HT2C mRNA was significantly increased in a dose-dependent manner in the cortex and the hypothalamus, as well as the 5HT3-receptor mRNA was in the hypothalamus. The 5HT6 mRNA level was increased in the forebrain cortex and the amygdala. Dopamine receptor mRNAs were only affected in the hypothalamus. In conclusion, this study provides evidence for a unique implication of serotonin rather than dopamine receptor mRNA levels, in response to repeated intermittent MDMA administration. We therefore suggest that serotonin regulated functions also primarily underlie repeated MDMA intake at rave parties.

L8 ANSWER 2 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2003157926 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12650952
TITLE: Investigating the role of dopaminergic and serotonergic candidate genes in obsessive-compulsive disorder.
AUTHOR: Hemmings Sian M J; Kinnear Craig J; Niehaus Dana J H; Moolman-Smook Johanna C; Lochner Christine; Knowles James A; Corfield Valerie A; Stein Dan J
CORPORATE SOURCE: MRC/US Centre for Molecular and Cellular Biology, University of Stellenbosch, P.O. Box 19063, 7505, Tygerberg, South Africa.. smjh@sun.ac.za
SOURCE: European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology, (2003 Mar) Vol. 13, No. 2, pp. 93-8.
Journal code: 9111390. ISSN: 0924-977X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 6 Apr 2003
Last Updated on STN: 13 May 2003
Entered Medline: 12 May 2003

AB There is increasing evidence that the aetiology of obsessive-compulsive disorder (OCD) has a marked genetic component, although the precise mechanism of inheritance is unclear. Clinical and pharmacological studies have implicated the serotonergic and dopaminergic systems in disease pathogenesis. This study investigated the role of attractive candidate genes in the serotonergic and dopaminergic pathways in the development of OCD. The distribution of selected polymorphic variants in the serotonin receptor type 2A and 1Dbeta (5-HT(2A), 5-HT(1Dbeta)), dopamine transporter (DAT), dopamine receptor type 4 (DRD4) and monoamine-oxidase A (MAO-A) genes were analysed in 71 OCD cases and 129 control individuals in the genetically homogeneous Afrikaner population, by means of case-control association studies. Although no statistically significant genotypic or allelic associations were detected, the data yielded interesting preliminary results that warrant further discussion and investigation.

L8 ANSWER 3 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2001300306 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11198050
TITLE: Manipulation of operant responding for an ethanol-paired conditioned stimulus in the rat by pharmacological alteration of the serotonergic system.
AUTHOR: Wilson A W; Costall B; Neill J C
CORPORATE SOURCE: Postgraduate Studies in Pharmacology, School of Pharmacy, University of Bradford, West Yorkshire, UK.. alex_w_wilson@sbphrd.com
SOURCE: Journal of psychopharmacology (Oxford, England), (2000) Vol. 14, No. 4, pp. 340-6.
Journal code: 8907828. ISSN: 0269-8811.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 4 Jun 2001
Last Updated on STN: 4 Jun 2001
Entered Medline: 31 May 2001

AB It is becoming increasingly clear that environmental stimuli play a critical role in the maintenance of drug taking behaviour. This has led to investigations into the neural mechanisms by which environmental stimuli can come to control behaviour using paradigms such as conditioned reinforcement. The majority of this work has involved the use of food-paired conditioned stimulus rodent paradigms. Relatively few studies have attempted to investigate the neuropharmacology of behaviour maintained by presentation of a stimulus paired with ethanol drinking. Several lines of research support an important role for brain serotonin (5-HT) neurotransmitter systems in the control of alcohol drinking behaviour. The aim of the present study was, initially, to establish a procedure in which rats respond for an ethanol-paired conditioned stimulus, and second, to study the effects of a range of serotonergic compounds previously shown to be effective in reducing oral ethanol self-administration, on responding for this conditioned stimulus. Results showed that the 5-HT releaser d-fenfluramine, the selective serotonin reuptake inhibitor fluoxetine, the 5-HT1A receptor agonist 8-hydroxy-2[di-n-propylamino]tetralin, the partial 5-HT1A receptor agonist buspirone, and the 5-HT1B/5-HT2C receptor agonist 1-(3-trifluoromethylphenyl)piperazine, but not the 5-HT2A/5-HT2C receptor agonist 1-(2,5-dimethoxy-4-iodophenylaminopropane)-2, selectively reduced responding on a lever leading to presentation of an ethanol paired conditioned stimulus. In addition the non-specific D1/D2 dopamine receptor antagonist haloperidol was active in this paradigm. Results are consistent with involvement of the dopaminergic and 5-HT systems, in particular activation of 5-HT1A and 5-HT1B receptor subtypes, in mediation of the conditioned or secondary reinforcing properties of ethanol.

L8 ANSWER 4 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2001170940 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11271402
TITLE: Receptor-mediated regulation of serotonin output in the rat dorsal raphe nucleus: effects of risperidone.
AUTHOR: Hertel P; Lindblom N; Nomikos G G; Svensson T H
CORPORATE SOURCE: Department of Physiology and Pharmacology, Karolinska Institutet, Stockolm, Sweden.
SOURCE: Psychopharmacology, (2001 Jan) Vol. 153, No. 3, pp. 307-14.
Journal code: 7608025. ISSN: 0033-3158.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 21 May 2001

Last Updated on STN: 21 May 2001
Entered Medline: 17 May 2001

AB OBJECTIVES: The present study was undertaken to characterize the regulation of serotonin (5-HT) efflux and neuronal activity in the dorsal raphe nucleus (DRN) as well as to examine the potential ability of the antipsychotic drug risperidone to interfere with these mechanisms. METHODS AND RESULTS: By using microdialysis in freely moving rats, it was found that administration of the alpha2 adrenoceptor antagonist idazoxan (0.25 mg/kg, SC), the 5-HT1B/D receptor antagonist GR 127,935 (1.0 mg/kg, SC) and risperidone (0.6 or 2.0 mg/kg, SC) increased 5-HT output in the DRN. Local DRN perfusion with GR 127,935 or risperidone via reversed dialysis (100 or 10-100 microM, respectively) enhanced 5-HT efflux in this area, whereas idazoxan (10-100 microM) failed to affect this parameter. Both systemic administration and reversed DRN dialysis of the D2/3 and 5-HT2A receptor antagonists raclopride (2.0 mg/kg, SC or 10-100 microM) and MDL 100,907 (1.0 mg/kg, SC or 10-100 microM), respectively, were without effect. Intraraphe dialysis of the 5-HT1B/D receptor agonist CP 135,807 (0.2 microM) decreased the efflux of 5-HT in the DRN, an effect which was antagonized by co-administration of either GR 127,935 or risperidone (10 and 3.3 microM, respectively). By using single-cell recording, it was found that administration of GR 127,935 (50-400 microg/kg, IV) decreased, whereas CP 135,807 (2.5-20 microg/kg, IV) increased firing of 5-HT cells in the DRN. CONCLUSIONS: Our findings suggest a regulatory role of local 5-HT1B/D receptors on 5-HT efflux as well as cell firing in the DRN and indicate that risperidone may interfere with the regulation of 5-HT availability in this area primarily via blockade of 5-HT1D receptors.

L8 ANSWER 5 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1999371966 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10443019
TITLE: 2-[4-[3-(4-aryl/heteroaryl-1-piperazinyl)propoxy]phenyl]-2H-benzotriazoles and their N-oxides as ligands for serotonin and dopamine receptors.
AUTHOR: Sparatore A; Goegan M; Cagnotto A; Sparatore F
CORPORATE SOURCE: Istituto di Chimica Farmaceutica e Tossicologica, Universita di Milano, Italy.. sparator@imiucca.csi.unimi.it
SOURCE: Farmaco (Societa chimica italiana : 1989), (1999 Jun 30) Vol. 54, No. 6, pp. 402-10.
Journal code: 8912641. ISSN: 0014-827X.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 10 Nov 1999

AB A small set of 2-{4-[3-(4-aryl/heteroaryl-piperazinyl]propoxy]phenyl}-2H-benzo tri azoles and corresponding N-oxides were prepared. The synthesized compounds were able to bind on some serotonin (5-HT1A, 5-HT2A) and dopamine (D2, D3) receptors, while displaying poor or no affinity for 5-HT1B, 5-HT2C, 5-HT3, and 5-HT4 subtypes. The strong contribution of the N-oxide function for the binding on 5-HT1A, D2 and D3 receptors is noteworthy. For 2-{4-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propoxy]phenyl}-2H-benzotr iazole- 1-oxide (4b), the binding constants (Ki) were 11.9 (5-HT1A) and 10.5 nM (D3). In a general pharmacological screening, the 2-{4-[3-(4-phenyl-1-piperazinyl)propoxy]phenyl}-2H-benzotriazole (3a) exhibited only very weak activities, with the exception of protecting mice from cyanide-induced hypoxia.

L8 ANSWER 6 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1998389363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9723970
TITLE: The role of alpha2-adrenoceptor antagonism in the anti-cataleptic properties of the atypical neuroleptic agent, clozapine, in the rat.
AUTHOR: Kalkman H O; Neumann V; Hoyer D; Tricklebank M D
CORPORATE SOURCE: Nervous Systems Research, Novartis Pharma AG, Basel, Switzerland.
SOURCE: British journal of pharmacology, (1998 Aug) Vol. 124, No. 7, pp. 1550-6.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 13 Nov 1998

AB 1. The mechanism underlying the anticataleptic properties of the atypical neuroleptic agent, clozapine, has been investigated in the rat. 2.The close structural analogues of clozapine, loxapine (0.1 mg kg(-1) s.c.) and iso-clozapine (1 and 3 mg kg(-1) s.c.) induced catalepsy in rats. In contrast, clozapine and the regio-isomer of loxapine, iso-loxapine (up to 10 mg kg(-1) s.c.) did not produce catalepsy, but at a dose of 1 mg kg(-1) significantly inhibited catalepsy induced by loxapine (0.3 mg kg(-1) s.c.). 3. Radioligand binding assays showed that cataleptogenic potential was most clearly predicted by the D2/5-HT1A, D2/5-HT1B/1D and D2/alpha2-receptor affinity (KD) ratios: i.e. 30-100-fold higher ratios were calculated for loxapine and iso-clozapine, whereas the ratios were less than 1 for clozapine and iso-loxapine. The ratios of affinities for D2 to 5-HT2A, 5-HT2C or D1 did not reflect the grouping of cataleptic and non-cataleptic compounds. 4. Co-treatment with the alpha2-adrenoceptor antagonists, yohimbine (1-10 mg kg(-1) s.c.), RX 821002 (1-10 mg kg(-1) s.c.) and MK-912 (0.3 and 1 mg kg(-1) s.c.) dose-dependently inhibited the cataleptic response to loxapine (0.3 mg kg(-1)). Yohimbine (1-10 mg kg(-1) s.c.) also dose-dependently inhibited the cateleptic response to haloperidol (0.3 mg kg(-1) s.c.). The alpha2-adrenoceptor antagonists had no effect per se. 5. Neither yohimbine (10 mg kg(-1)) nor RX821002 (3 mg kg(-1)) altered the cataleptic response to the D1 receptor antagonist, SCH 23390 (1 mg kg(-1) s.c.), while, like clozapine, both compounds abolished the response to the 5-HT2A receptor antagonist, MDL 100,151 (3 mg kg(-1) s.c.). 6. The present data strongly implicate alpha2-adrenoceptor blockade in the anticataleptic properties of clozapine and suggest that its lack of extrapyramidal side effects in the clinic may also be a consequence of this property.

L8 ANSWER 7 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1998316312 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9651340
TITLE: Cross-talk between 5-hydroxytryptamine receptors in a serotonergic cell line. Involvement of arachidonic acid metabolism.
AUTHOR: Tournois C; Mutel V; Manivet P; Launay J M; Kellermann O
CORPORATE SOURCE: Differenciation Cellulaire, CNRS URA 1960, Institut Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15, France.
SOURCE: The Journal of biological chemistry, (1998 Jul 10) Vol. 273, No. 28, pp. 17498-503.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 17 Aug 1998
Last Updated on STN: 17 Aug 1998
Entered Medline: 6 Aug 1998

AB The study of signaling cascades and of functional interactions between 5-hydroxytryptamine (5-HT) receptor pathways with heterogenous brain cell populations remains an arduous task. We took advantage of a serotonergic cell line to elucidate cross-talks between 5-HT receptors and to demonstrate the involvement of two 5-HT2 receptor subtypes in the regulation of 5-HT1B/1D function. The inducible 1C11 cell line has the unique property of acquiring within 4 days a complete serotonergic phenotype (1C11* cells), including three 5-HT receptors. 5-HT1B/1D and 5-HT2B receptors are expressed since day 2 of the serotonergic differentiation while 5-HT2A receptors are induced at day 4. We first established that 5-HT2B receptors are coupled with the phospholipase A2 (PLA2)-mediated release of arachidonic acid (AA) and that the activation of 5-HT2B receptors in 1C11* d2 cells inhibits the 5-HT1B/1D receptor function via a cyclooxygenase-dependent AA metabolite. At day 4, this 5-HT2B-mediated inhibition of the 5-HT1B/1D function can be blocked upon concomitant 5-HT2A activation although a 5-HT2A/PLA2 positive coupling was evidenced. This suggests the existence in 1C11*d4 cells of pathway(s) for 5-HT2A receptors, distinct from PLC and PLA2. Finally, this study reveals the antagonistic roles of 5-HT2A and 5-HT2B receptors in regulating the function of 5-HT1B/1D, a receptor involved in neuropsychiatric disorders and migraine pathogenesis.

L8 ANSWER 8 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1998230395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9570468
TITLE: Cataleptogenic effect of subtype selective 5-HT receptor antagonists in the rat.
AUTHOR: Kalkman H O; Neumann V; Nozulak J; Tricklebank M D
CORPORATE SOURCE: Nervous System Research, Novartis Pharma Inc., Basel, Switzerland.
SOURCE: European journal of pharmacology, (1998 Feb 19) Vol. 343, No. 2-3, pp. 201-7.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 18 Jun 1998
Last Updated on STN: 18 Jun 1998
Entered Medline: 9 Jun 1998

AB 5-HT receptor antagonists with selectivity for 5-HT1A WAY-100635 (N-[2-[-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-(2-pyridinyl)cyclohe xanecarboxamide), 5-HT1B GR 127935 (N-[methoxy-3-(4-methyl-1-piperazinyl)phenyl]-2'-methyl-4'(5-methyl-1,2, 4-oxadiazol-3-yl)[1,1-biphenyl]-4-carboxamide x HCl), 5-HT2C SB 200646A (N-(1-methyl-5-indolyl)-N'-(3-pyridyl)urea x HCl) and 5-HT2A (ketanserin, fananserin and MDL 100,151 ((+/-)-alpha-(2,3-dimethoxyphenyl)-1-[2-(4-fluorophenyl)ethyl]-4-pipe ridinemethanol) receptors were tested for cataleptogenic responses in rats. WAY-100635 (0.1-3 mg/kg, s.c.), ketanserin (0.1-3 mg/kg, s.c.), MDL 100,151 (0.3-3 mg/kg, s.c.) and fananserin (RP 62203; 3 mg/kg, s.c.) induced a significant catalepsy. GR 127935 (1 mg/kg, s.c.), SB 200646A (without effect per se at 10 mg/kg, s.c.) and MDL 100,151 (0.3 mg/kg, s.c.) did not inhibit the cataleptic response to the dopamine D2 receptor antagonist, loxapine (0.3 mg/kg, s.c.). Catalepsy induced by MDL 100,151 (3 mg/kg) was blocked by co-treatment with clozapine, but not by SB 200646A (both at 10 mg/kg, s.c.). Although clozapine displays significant affinity to 5-HT1A, 5-HT1B, 5-HT2A and 5-HT2C receptors, the present results suggest that blockade of these receptors is not responsible for clozapine's anticataleptic activity.

L8 ANSWER 9 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1998149351 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9489707
TITLE: Serotonin neural adaptations to ontogenetic loss of dopamine neurons in rat brain.
AUTHOR: Kostrzewa R M; Reader T A; Descarries L
CORPORATE SOURCE: Department of Pharmacology, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, USA.
SOURCE: Journal of neurochemistry, (1998 Mar) Vol. 70, No. 3, pp. 889-98. Ref: 94
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19 Mar 1998
Last Updated on STN: 19 Mar 1998
Entered Medline: 12 Mar 1998

AB In rat, the neonatal destruction of nigrostriatal dopamine (DA) neurons by intracerebral administration of 6-hydroxydopamine entails dramatic changes in serotonin (5-hydroxytryptamine, 5-HT) as well as DA function. Most striking is the 5-HT hyperinnervation of the adult neostriatum, associated with increases in density of various 5-HT receptor subtypes and enhanced neuronal responsiveness to the iontophoretic application of 5-HT and its 5-HT(1B/2C) and 5-HT(2A/2C) receptor agonists, m-chlorophenylpiperazine and iododimethoxyphenylaminopropane. The topographical distribution of these changes is consistent with up-regulation and/or increased production and transport of 5-HT1B and 5-HT2A receptors by the neostriatal projection neurons, as confirmed for the 5-HT2A receptor in a recent in situ hybridization study. It is interesting that this study has also shown that increases in both 5-HT2A binding and mRNA level were abolished by chronic pretreatment with the DA agonists, apomorphine and SKF 38393, suggesting a regulatory influence of DA in the expression of this 5-HT receptor. D1 receptor binding is known to be slightly reduced in the rostral neostriatum of these rats, a down-regulation apparently imputable to a reduced rate of synthesis of the receptor. In contrast, D2 receptor binding is increased throughout the DA-denervated and 5-HT-hyperinnervated neostriatum, perhaps due to some posttranscriptional modifications. Stereotyped and motor behaviors induced by systemic treatment with D1 and D2 agonists are markedly enhanced in these rats (behavioral supersensitivity), although priming is commonly required to unmask a latent D1 supersensitivity. In the case of oral activity, however, overt behavioral supersensitivity is induced by D1 as well as D2 agonists. Moreover, there is overt supersensitivity of oral activity in response to the 5-HT receptor agonist m-chlorophenylpiperazine, which is presumably imputable to 5-HT2C receptors and may be demonstrated even in the absence of supersensitivity to D1 receptor agonist. 5-HT adaptations, therefore, seem to play a role not only in the abnormal spontaneous behavior, but also in the behavioral supersensitivity to 5-HT as well as DA receptor agonists in these rats.

L8 ANSWER 10 OF 15 MEDLINE on STN
ACCESSION NUMBER: 97021512 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8867872
TITLE: Evidence that m-chlorophenylpiperazine-induced hyperthermia in rats is mediated by stimulation of 5-HT2C receptors.

AUTHOR: Mazzola-Pomietto P; Aulakh C S; Wozniak K M; Murphy D L
CORPORATE SOURCE: Laboratory of Clinical Science, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892-1264, USA.
SOURCE: Psychopharmacology, (1996 Feb) Vol. 123, No. 4, pp. 333-9. Journal code: 7608025. ISSN: 0033-3158.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19 Dec 1996
Last Updated on STN: 19 Dec 1996
Entered Medline: 15 Nov 1996

AB Intraperitoneal administration of m-chlorophenylpiperazine (m-CPP) to Wistar rats produced hyperthermia with a peak effect at 30 min. Pretreatment with low doses of metergoline (5-HT1/5-HT2 antagonist), mesulergine and mianserin (5-HT2C/5-HT2A antagonists) blocked m-CPP-induced hyperthermia. Pretreatment with propranolol (beta-adrenergic receptor antagonist that also has binding affinity for 5-HT1A, 5-HT1B and 5-HT2B sites), yohimbine (alpha 2-noradrenergic antagonist that also has binding affinity for 5-HT2B sites), MDL-72222 or ondansetron (5-HT3 antagonists) did not attenuate m-CPP-induced hyperthermia. Only high doses of ketanserin, LY-53857 and ritanserin (5-HT2A/5-HT2C antagonists) as well as spiperone (5-HT1A/5-HT2A/D2 antagonist) attenuated m-CPP-induced hyperthermia. Daily administration of m-CPP produced complete tolerance to its hyperthermic effect by day 5. However, there was no cross-tolerance to 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI, a 5-HT2A agonist that also has high affinity for 5-HT2C receptors)-induced hyperthermia. m-CPP-induced increases in temperature were found to be significantly less in the Fawn-Hooded (FH) rat strain as compared to the Wistar rat strain; in prior studies, FH rats have been found to be subsensitive to other 5-HT2C-mediated pharmacologic responses. Altogether, these findings suggest that m-CPP-induced hyperthermia in rats is mediated by selective stimulation of 5-HT2C receptors.

L8 ANSWER 11 OF 15 MEDLINE on STN
ACCESSION NUMBER: 95316519 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7796132
TITLE: Short and long-term changes in dopamine and serotonin receptor binding sites in amphetamine-sensitized rats: a quantitative autoradiographic study.
AUTHOR: Bonhomme N; Cador M; Stinus L; Le Moal M; Spampinato U
CORPORATE SOURCE: INSERM U. 259, Universite de Bordeaux II, France.
SOURCE: Brain research, (1995 Mar 27) Vol. 675, No. 1-2, pp. 215-23. Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 17 Aug 1995
Last Updated on STN: 17 Aug 1995
Entered Medline: 3 Aug 1995

AB The biochemical changes in DA and 5HT systems were investigated in amphetamine (AMPH)-sensitized rats, 1 and 15 days after cessation of treatment (5 mg/kg AMPH, i.p., twice a day for 6 days). At both times, AMPH-treated rats exhibited behavioral sensitization, as revealed by an enhancement of the stereotypic response to a challenge dose of 2 mg/Kg, ip. AMPH. Basal dopamine (DA) and serotonin (5-HT) metabolism was not significantly modified in different brain areas of AMPH-sensitized rats. Quantitative autoradiographic analysis of DA and serotonin 5-HT receptor subtypes was performed in the following brain regions: medial prefrontal cortex, nucleus accumbens, striatum, substantia nigra, ventral tegmental area, dorsal and median raphe nuclei. A significant increase of [3H]SCH 23390 binding to D1 DA receptors was observed in the substantia nigra pars reticulata 1 day but not 15 days after the cessation of AMPH treatment, whereas [3H]8-OH-DPAT binding to 5-HT1A sites was found to be significantly enhanced in the dorsal raphe nucleus at both time points. No change in D2 DA nor in 5-HT1B or 5-HT2A receptors was found in any of the brain structures examined at either time point. The obtained results suggest that DA and 5-HT systems are differently and time-dependently involved in AMPH-induced behavioral sensitization.

L8 ANSWER 12 OF 15 MEDLINE on STN
ACCESSION NUMBER: 95273535 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7753967
TITLE: Evidence that 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI)-induced hyperthermia in rats is mediated by stimulation of 5-HT2A receptors.
AUTHOR: Mazzola-Pomietto P; Aulakh C S; Wozniak K M; Hill J L; Murphy D L
CORPORATE SOURCE: Laboratory of Clinical Science, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892, USA.
SOURCE: Psychopharmacology, (1995 Jan) Vol. 117, No. 2, pp. 193-9. Journal code: 7608025. ISSN: 0033-3158.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 29 Jun 1995
Last Updated on STN: 29 Jun 1995
Entered Medline: 22 Jun 1995

AB The effects of various 5-HT receptor subtype-selective antagonists were studied on phenylisopropylamine hallucinogen 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI)-induced hyperthermia in Wistar rats, in an attempt to characterize the 5-HT receptor subtype mediating DOI-induced hyperthermia. Intraperitoneal administration of DOI to rats produced hyperthermia with a peak effect at 60 min. Pretreatment with propranolol (beta-adrenoceptor antagonist that also has binding affinity for 5-HT1A, 5-HT1B and 5-HT2C sites), MDL-72222 or ondansetron (5-HT3 antagonists) did not attenuate DOI-induced hyperthermia. In contrast, pretreatment with metergoline (5-HT1/5-HT2 antagonist), ketanserin, LY53857, mesulergine, mianserin and ritanserin (5-HT2C/5-HT2A antagonists), as well as spiperone (5-HT1A/5-HT2A/D2 antagonist), significantly attenuated DOI-induced hyperthermia. Furthermore, daily administration of DOI (2.5 mg/kg per day) for 17 days did not produce either tolerance to its hyperthermic effect or modify m-CPP-induced hyperthermia in rats. These findings suggest that DOI-induced hyperthermia in rats is mediated by stimulation of 5-HT2A receptors.

L8 ANSWER 13 OF 15 MEDLINE on STN
ACCESSION NUMBER: 95055070 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7965707
TITLE: Role of various 5-HT receptor subtypes in mediating neuroendocrine effects of 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) in rats.
AUTHOR: Aulakh C S; Mazzola-Pomietto P; Hill J L; Murphy D L
CORPORATE SOURCE: Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland.
SOURCE: The Journal of pharmacology and experimental therapeutics, (1994 Oct) Vol. 271, No. 1, pp. 143-8.

Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 10 Jan 1995
Last Updated on STN: 10 Jan 1995
Entered Medline: 25 Nov 1994

AB The phenylisopropylamine hallucinogen 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) produced dose-related increases in plasma concentrations of prolactin, adrenocorticotropic hormone (ACTH) and corticosterone but not growth hormone in rats. Pretreatment with metergoline (serotonin, 5-HT1/5-HT2 antagonist), ritanserin and mianserin (5-HT2A/5-HT2C antagonists) significantly attenuated DOM-induced increases in prolactin, ACTH and corticosterone, whereas mesulergine (5-HT2A/5-HT2C antagonist) pretreatment significantly attenuated DOM-induced increases in plasma prolactin and ACTH but not corticosterone. Pretreatment with propranolol (beta adrenoceptor antagonist that also has high binding affinity for 5-HT1A, 5-HT1B and 5-HT2C sites), MDL-72222 and ondansetron (5-HT3 antagonists) attenuated DOM's effect on plasma prolactin, but did not attenuate DOM-induced increases in either ACTH or corticosterone. On the other hand, spiperone (5-HT1A/5-HT2A/D2 antagonist) pretreatment significantly attenuated DOM-induced increases in ACTH but not corticosterone. These findings demonstrate involvement of 5-HT2A/5-HT2C and 5-HT3 receptors in mediating DOM-induced increases in plasma prolactin, whereas DOM-induced increases in ACTH appear to be mediated by stimulation of 5-HT2A receptors. DOM-induced corticosterone secretion appears to be mediated by stimulation of 5-HT2A and/or 5-HT2C receptors. DOM does not affect growth hormone secretion in rats.

L8 ANSWER 14 OF 15 MEDLINE on STN
ACCESSION NUMBER: 94308931 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8035308
TITLE: Evidence that 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane-induced hypophagia and hyperthermia in rats is mediated by serotonin-2A receptors.
AUTHOR: Aulakh C S; Mazzola-Pomietto P; Wozniak K M; Hill J L; Murphy D L
CORPORATE SOURCE: Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland.
SOURCE: The Journal of pharmacology and experimental therapeutics, (1994 Jul) Vol. 270, No. 1, pp. 127-32.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 25 Aug 1994
Last Updated on STN: 25 Aug 1994
Entered Medline: 15 Aug 1994

AB The administration of various doses of the phenylisopropylamine hallucinogen 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) to rats produced dose-related decreases in 1-hr food intake in a food-restricted paradigm and in locomotor activity. DOM also produced dose-related increases in temperature. Pretreatment with propranolol [a beta adrenoceptor antagonist that also has high binding affinity for serotonin (5-HT) 5-HT1A, 5-HT1B and 5-HT2C sites], bemesetron or ondansetron (5-HT3 antagonists) did not attenuate either DOM-induced hypophagia or hyperthermia. In contrast, pretreatment with metergoline (a 5-HT1/5-HT2 antagonist) and ritanserin (a 5-HT2A /5-HT2C antagonist) significantly attenuated both DOM-induced hypophagia and hyperthermia. However, pretreatment with mesulergine (a 5-HT2C/5-HT2A antagonist) significantly attenuated DOM-induced hyperthermia but not hypophagia. On the other hand, spiperone (5-HT1A/5-HT2A/D2 antagonist) pretreatment significantly attenuated DOM-induced hyperthermia but accentuated DOM-induced hypophagia. Daily administration of DOM (1.0 mg kg-1 day-1) produced complete tolerance to its hypophagic effect by day 4 but did not produce cross-tolerance to m-chlorophenylpiperazine-induced hypophagia. In contrast, daily administration of DOM for 7 days did not produce either tolerance to its hyperthermic effect or modify m-chlorophenylpiperazine-induced hyperthermia in rats. These findings suggest that DOM-induced hypophagia and hyperthermia in rats are mediated by stimulation of 5-HT2a receptors.

L8 ANSWER 15 OF 15 MEDLINE on STN
ACCESSION NUMBER: 94138685 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8306109
TITLE: Evidence that RU 24969-induced locomotor activity in C57/B1/6 mice is specifically mediated by the 5-HT1B receptor.
AUTHOR: Cheetham S C; Heal D J
CORPORATE SOURCE: Boots Pharmaceuticals Research Department, Nottingham.
SOURCE: British journal of pharmacology, (1993 Dec) Vol. 110, No. 4, pp. 1621-9.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 30 Mar 1994
Last Updated on STN: 30 Mar 1994
Entered Medline: 17 Mar 1994

AB 1. The behavioural effects of the 5-HT1B receptor agonists, RU 24969 and CGS 12066B, have been investigated in C57/B1/6 mice. 2. RU 24969 (1-30 mg kg-1) produced intense and prolonged hyperlocomotion and other behavioural changes. 3. CGS 12066B caused similar effects, but they were much less pronounced, inconsistent and transient irrespective of whether this drug was given i.p. (1-15 mg kg-1) or i.c.v. (0.2-40 micrograms). However, CGS 12066B (7.5 and 15 mg kg-1) caused a dose-related inhibition of RU 24969 (7.5 mg kg-1)-induced hyperlocomotion indicating that the former is a 5-HT1B partial agonist. 4. RU 24969 (7.5 mg kg-1 i.p.)-induced hyperlocomotion was inhibited by the (-)-, but not (+)-isomers of pindolol (4 mg kg-1) and propranolol (20 mg kg-1) but not by metoprolol (10 mg kg-1) or ICI 118,551 (5 mg kg-1), consistent with an involvement of 5-HT1A or 5-HT1B receptors. 5. The response was not altered by the selective 5-HT1A receptor antagonist, WAY 100135 (5 mg kg-1, s.c.), the 5-HT2A/5-HT2C receptor antagonist, ritanserin (0.1 mg kg-1), the selective 5-HT3 receptor antagonist, ondansetron (1 mg kg-1) or the non-selective 5-HT receptor antagonists methysergide (3 mg kg-1) and metergoline (3 mg kg-1). 6. Although spiroxatrine (0.1 mg kg-1) and ketanserin (1 mg kg-1) inhibited RU 24969-induced hyperlocomotion, these effects were probably due to antagonism of dopamine D2 receptors and alpha 1-adrenoceptors respectively. (ABSTRACT TRUNCATED AT 250 WORDS)

=>

10/800,328

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("5157034").PN.	USPAT	OR	OFF	2007/04/09 09:38
L2	877056	514/217.07 OR 514/249 OR 540/599 IR 544/349	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/04/09 09:39
L3	17	L2 AND (PYRIDO[1,2-A]PYRAZINE OR PYRIDO[1,2-A]PYRAZIN)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/04/09 09:40